

Kuo, George v. 1 Confidential

1 IN THE UNITED STATES DISTRICT COURT  
2 IN AND FOR THE NORTHERN DISTRICT OF CALIFORNIA  
3 CHIRON CORPORATION,  
4 Plaintiff,  
5 vs. CIVIL ACTION NO.  
6 F. HOFFMANN-LA ROCHE LTD. 98-0315 (CV)  
7 HOFFMANN-LA ROCHE INC.,  
8 ROCHE MOLECULAR SYSTEMS, INC.,  
9 ROCHE DIAGNOSTIC SYSTEMS, INC.  
10 and DANIEL W. BRADLEY,  
11 Defendants.

12  
13 CONFIDENTIAL  
14 DEPOSITION OF GEORGE KUO, Ph.D  
15 Monday, November 8, 1999  
16 VOLUME I  
17 Pages 1 to 244  
18 REPORTED BY: FRANCES ANN WEINROB, C.S.R.  
19 CERTIFIED REALTIME REPORTER  
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22  
23  
24  
25

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1 A P P E A R A N C  
2  
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I N D E X		
2	EXAMINATION BY:	PAGE
4	Mr. Rabinowitz	8
5		
6	LET IT BE NOTED that all exhibits are	
7	separately bound.	
8		
9	DEPOSITION EXHIBITS:	
10	200 Copy, U.S. Patent 5,714,596	93
11	(62 pages)	
12		
13	201 Copy, U.S. Patent Application, Serial No.	129
14	08/040,564, filed 3/31/93	
15	(15 pages)	
16		
17	202 Copy, U.S. Patent Application Amendment,	134
18	Serial No. 08/040,564, filed 3/31/93	
19	(15 pages)	
20		
21	203 Copy, U.S. Patent Application Transmittal	139
22	Letter, from Gladys H. Monroy	
23	(108 pages)	
24		
25		

1 I N D E X  
 2 DEPOSITION EXHIBITS: PAGE  
 3 204 Copy, U.S. Patent 5,350,671 234  
 4 (201 pages)

1 BE IT REMEMBERED that, pursuant to Notice,  
 2 and on Monday, November 8, 1999, commencing at the hour  
 3 of 9:08 a.m. thereof, at the Law Offices of Heller,  
 4 Ehrman, White & McAuliffe, 333 Bush Street, Conference  
 5 Room 3105, San Francisco, California, before me,  
 6 FRANCES A. WEINROB, a Certified Shorthand Reporter and  
 7 a Certified Realtime Reporter, there personally  
 8 appeared  
 9 GEORGE KUO, Ph.D.,  
 10 called as a witness by defendants F. Hoffmann-La Roche  
 11 Ltd, Roche Molecular Systems, Inc., and Roche  
 12 Diagnostic Systems, Inc., and who, being first duly  
 13 sworn, was thereupon examined and testified as  
 14 hereinafter set forth.

15 THE VIDEOGRAPHER: Good morning.  
 16 This marks the beginning of Videotape 1 in  
 17 the deposition of Dr. George Kuo, Ph.D., in the matter  
 18 of Chiron Corporation v F. Hoffmann-La Roche Ltd, et  
 19 al., in the United States District Court for the  
 20 Northern District of California, Case No. 98-0315 (CW).  
 21 Today's date is November the 8th, 1999 and  
 22 the time is 9:08. The location of this deposition is  
 23 333 Bush Street, San Francisco, California.

24 The deposition was noticed by the attorneys  
 25

1 for Hoffmann-La Roche Ltd, Roche Molecular Systems,  
 2 Incorporated and Roche Diagnostic Systems,  
 3 Incorporated, and the videotape is being produced on  
 4 behalf of the same.

5 The video operator is Vincent Brown, a  
 6 California Notary Public for the County of San  
 7 Francisco, employed by Dan Mottaz Video Productions at  
 8 402 Dewey Boulevard, San Francisco, California 94116,  
 9 area code (415) 731-1300.

10 Our court reporter today is Fran Weinrob  
 11 with the reporting firm of Grossman & Cotter.

12 Would counsel present please identify  
 13 themselves and state whom they represent.

14 MR. RABINOWITZ: Stephen Rabinowitz, Pennie  
 15 & Edmonds, LLP for the Roche defendants.

16 MR. HERRIDGE: Peter Herridge, Pennie &  
 17 Edmonds, LLP for the Roche defendants.

18 MR. PERHACS: Pablo Perhacs, Pennie &  
 19 Edmonds, LLP, also for the La Roche defendants.

20 MR. GRECO: Richard Greco, Kay,  
 21 Scholer, Fierman, Hays & Handler, LLP, for Chiron  
 22 Corporation, the plaintiff.

23 THE VIDEOGRAPHER: If there are no  
 24 stipulations at this time, may the reporter swear in

1 the witness.

2 MR. RABINOWITZ: Certainly, please go ahead.  
 3 (Witness sworn.)

4 EXAMINATION BY MR. RABINOWITZ

5 MR. RABINOWITZ: Q. Good morning, doctor.  
 6 A. Good morning.  
 7 Q. Would you please state your full name for  
 8 the record.

9 A. Yes. My name is George Kuo.

10 Q. Thank you. And the pronunciation is "Kuo"?

11 A. That is okay.

12 Q. I'll try to get that right.

13 My name is Stephen Rabinowitz. I'll be  
 14 asking questions at your deposition here today, and the  
 15 questions and your answers will be recorded by Fran  
 16 Weinrob, the court reporter.

17 I would ask you to speak up and to answer  
 18 orally because the reporter can't transcribe hand  
 19 gestures and nodding or shaking of your head.

20 Is that okay?

21 A. Sure.

22 Q. If for any reason you don't understand the  
 23 question, please let me know and I'll try and rephrase  
 24 it more clearly. Okay?

1 A. Sure.  
 2 Q. And if at any time you need a break, please  
 3 let us know. We'll deal with whatever question is  
 4 pending, and then we'll schedule a break as soon as  
 5 possible. Okay?  
 6 A. Yes.  
 7 Q. Also, if you've given an answer and you  
 8 subsequently realize that you have more information  
 9 that's responsive to the question or if you need to  
 10 clarify the answer you've given, please let us know and  
 11 once we've dealt with whatever question is then  
 12 pending, we'll deal with -- we'll give you an  
 13 opportunity to clarify your answer or supplement it at  
 14 that time. Okay?  
 15 A. Yes.  
 16 Q. In addition, if while you're answering a  
 17 question you think of some documents that might enable  
 18 you to remember information that's responsive to the  
 19 question, please tell us and we'll see if we have the  
 20 documents here or, if we don't have them here, if we  
 21 can get them. Okay?  
 22 A. Okay.  
 23 Q. Dr. Kuo, your English is fluent, is it?  
 24 A. I guess so.  
 25

1 Q. Your higher education has been in English?  
 2 A. No, I educated in Taiwan.  
 3 Q. I see. You do your scientific work in  
 4 English. Is that right?  
 5 A. Yes.  
 6 Q. And you write your papers, your scientific  
 7 papers, in English. Correct?  
 8 A. Correct.  
 9 Q. Right. Is there any reason that you might  
 10 have difficulty in understanding questions today or in  
 11 answering them?  
 12 A. I don't think so.  
 13 Q. You're not taking any medications or any  
 14 drug of any kind that might impair your ability to  
 15 understand my questions or to answer them accurately?  
 16 A. No.  
 17 Q. No. Have you ever been deposed before?  
 18 A. Yes.  
 19 Q. In what cases have you been deposed?  
 20 A. In hepatitis C protease case.  
 21 Q. And who were the parties in that case?  
 22 A. You mean the company's name?  
 23 Q. Yes.  
 24 A. It's Eli Lilly.  
 25

1 Q. I beg your pardon?  
 2 A. The party is Eli Lilly -- right? -- is the  
 3 company.  
 4 MR. GRECO: I think he said "Eli  
 5 Lilly."  
 6 MR. RABINOWITZ: Oh, Eli Lilly.  
 7 Q. This was Chiron pursuing Eli Lilly, was it?  
 8 A. Agouron, Vertex and Gilead.  
 9 Q. So that's Chiron versus Eli Lilly & Co,  
 10 right? Chiron versus Agouron?  
 11 A. Yes.  
 12 Q. Chiron versus Vertex?  
 13 A. Yes.  
 14 Q. And Chiron versus Gilead?  
 15 A. Yes.  
 16 Q. Is that G-I-L-E-A-D?  
 17 A. I think so.  
 18 Q. Right. Were you deposed once in relation to  
 19 all those cases, or were you deposed more than once?  
 20 A. Only once.  
 21 Q. Once. What was the subject matter of the  
 22 patents that were being litigated in that case?  
 23 A. This is hepatitis C protease.  
 24 Q. Okay. And, generally, what was the -- what  
 25

1 did your testimony relate to in the deposition there?  
 2 A. It related to hepatitis C protease.  
 3 Q. Did you discuss the definition of hepatitis  
 4 C virus?  
 5 MR. GRECO: Object to the form.  
 6 Answer if you recall.  
 7 THE WITNESS: Yes.  
 8 MR. RABINOWITZ: Q. Did you discuss  
 9 antibodies against hepatitis C virus or any hepatitis C  
 10 virus peptides?  
 11 A. Yes.  
 12 Q. So you testified about antibodies to  
 13 hepatitis C virus or peptides encoded by hepatitis C  
 14 virus. Correct?  
 15 A. Plus something else.  
 16 Q. What else did you testify about?  
 17 A. The genome, the protein, and other things.  
 18 Q. I see. Apart from the Chiron cases  
 19 involving Eli Lilly, Agouron, Vertex and Gilead, have  
 20 you ever given deposition testimony in any other  
 21 litigation?  
 22 A. In the United States?  
 23 Q. In the United States or elsewhere.  
 24 A. Only in -- deposition is confined in the  
 25

1      United States.

2      Q.        So besides those cases, you've never given a  
3      deposition in any other case? I'll ask you separately  
4      about in-court testimony in a moment.5      MR. GRECO:    I think that's what the  
6      confusion is.

7      MR. RABINOWITZ: Yes.

8      Q.        I'm asking specifically about depositions at  
9      the moment.

10     A.       No, that's it.

11     Q.       Right. Now, as for any other evidence  
12    you've given under oath besides depositions, have you  
13    ever testified under oath --

14     A.       I don't understand your question.

15     Q.       Have you ever given evidence in court?

16     A.       In what respect?

17     Q.       In any litigation at all.

18     A.       I still don't understand the question.

19     Q.       Have you ever testified in a court of law?

20     A.       In relate to a patent or relate to something  
21    else?

22     Q.       In relation to anything whatsoever.

23     A.       No, I didn't.

24     Q.       Have you ever been a witness in any

25

1      litigation?

2      A.       No. I don't recall.

3      Q.       Do you recall that Chiron was involved in a  
4      litigation against Organon?

5      A.       That is in U.K.?

6      Q.       In the U.K. and perhaps elsewhere.

7      A.       Yes.

8      Q.       Were you a witness in that case?

9      A.       In the court, yes.

10     Q.       Okay. Are there any --

11     So I'm now trying to ask about any cases,  
12    including, for example, Chiron versus Organon in the  
13    U.K. Any case in any country where you've been a  
14    witness.15     A.       You have to define the question clearly for  
16    me, because your question is very, very broad. So you  
17    want to relate to the hepatitis C or something else?18     Q.       I'm talking about relating to anything. I'm  
19    just asking you to give me a list of all the cases that  
20    you've been a witness or given testimony in, no matter  
21    what they relate to and no matter where they occurred.

22     A.       Yes, in the U.K., yes. The Organon, yes.

23     Q.       The Organon case.

24     A.       Yes.

25

1      Q.       Any other cases?

2      A.       I don't recall.

3      Q.       Would you please describe for me your  
4      educational background since high school.5      A.       I get my bachelor degree from National  
6      Taiwan University, and my Ph.D. from Albert Einstein  
7      College of Medicine in molecular biology.8      Q.       Any other formal education after high  
9      school?10     A.       I did my postdoc at Yale, and I work at UCSF  
11    School of Medicine before I join Chiron.12     Q.       And apart from National Taiwan University,  
13    Albert Einstein College of Medicine, a postdoc at Yale,  
14    working at UCSF School of Medicine, any other education  
15    after high school, or is that the lot?16     A.       I worked at College of Medicine, National  
17    Taiwan University after I got my bachelor degree.

18     Q.       And anything else?

19     A.       No.

20     Q.       Okay. Let's go back to your bachelor's  
21    degree at National Taiwan University. What year did  
22    you begin your studies there?

23     A.       1957.

24     Q.       And what year did you end your --

25

1      A.       '61.

2      Q.       Did you graduate in 1961?

3      A.       Correct.

4      Q.       And what was your major concentration  
5      in university?

6      A.       In science.

7      Q.       Did you subspecialize in --

8      A.       No, bachelor of science.

9      Q.       So that included physics?

10     A.       Yes.

11     Q.       And chemistry?

12     A.       Yes.

13     Q.       Biology?

14     A.       Yes.

15     Q.       Molecular biology?

16     A.       No.

17     Q.       Immunology?

18     A.       Yes.

19     Q.       Did you do as an undergraduate any bench  
20    work in the laboratory?

21     A.       Yes.

22     Q.       What projects were you involved in as an  
23    undergraduate student?

24     A.       This relate to microbiology and immunology.

25

1 Q. What was the -- what projects did you have  
2 in microbiology?

3 A. Try to find out the half-life for  
4 antibiotics in rabbit.

5 (Reporter interruption.)

6 THE WITNESS: In the rabbit animal,  
7 rabbit.

8 MR. RABINOWITZ: Q. Any other microbiology  
9 projects?

10 A. That already took my whole year's work.

11 Q. Okay. Did you work with viruses at that  
12 time?

13 A. Yes.

14 Q. What work did you do with viruses?

15 A. Well, that is just in the class.

16 Q. And what viruses did you work with?

17 A. It's a medical microbiology, so cover all  
18 the biology relate to the human.

19 Q. I see. Did you do any experimental work  
20 with viruses at that time?

21 A. Experiment is doing the lab work. So I  
22 experiment.

23 Q. What kinds of experiments did you do that  
24 involved viruses as an undergraduate?

25

1 A. Titered, for example, influenza virus and so  
2 on.

3 Q. What other viruses did you work with besides  
4 influenza virus?

5 A. After I graduated, I worked with polyoma  
6 virus SV-40.

7 Q. Where was that?

8 A. Adenovirus.

9 Initial time at University Medical School.

10 Q. Polyoma SV-40?

11 A. SV-40.

12 Q. Right. Any other viruses?

13 A. Adenovirus.

14 (Reporter interruption.)

15 MR. RABINOWITZ: I think we'll have to spell  
16 them.

17 Q. Could you spell adenovirus?

18 A. A-D-N-O --

19 Q. Is that A-D-E-N-O-V-I-R-U-S?

20 A. Yes.

21 Q. Okay. Any other viruses?

22 A. I don't recall.

23 Q. And besides titrating antibiotics in rabbits  
24 and working with the viruses you've named, were there  
25

1 any other projects as an undergraduate in microbiology?

2 A. You have to define the question for me and  
3 then I can answer, because this is a whole year class.  
4 So you want me to spend whole day trying to tell you --

5 What kind of virus do you want me to answer?

6 You ask me question, I say yes or no. I think that is  
7 easier for me.

8 Q. I think it would take a very long time if we  
9 confined this to purely yes or no questions.

10 I'm interested in getting an overview of  
11 your exposure to bench science as an undergraduate. So  
12 you told me that you titrated antibiotics in rabbits  
13 and --

14 A. Textbook we use in medical microbiology is  
15 the textbook by Zinzer, so that is a very well-known  
16 medical textbook. So in there we have to learn all the  
17 virus that's in there, then we have to do some  
18 experiment.

19 Q. Okay, and it's the experiments you did that  
20 I'm focusing on. I'm not asking about the content of  
21 the instructional course. I'm asking about the  
22 experiments that you actually did in the laboratories  
23 while you were at --

24 A. Mostly I don't recall. If you ask the

25

1 simple question, I can answer it.

2 Q. Okay. Well, answer as far as you can  
3 recollect, and, you know, if you don't recollect  
4 anything else, then you'll just give that answer and  
5 that will be fine.

6 You said that you did laboratory work in  
7 immunology as an undergraduate at National University  
8 of Taiwan. What projects did you have in immunology  
9 there?

10 A. I tried to get the polyclonal antibody.  
11 (Reporter interruption.)

12 MR. GRECO: Polyclonal antibody.  
13 P-O-L-Y-C-L-O-N-A-L, antibody.

14 MR. RABINOWITZ: Q. Against what did you  
15 try and raise polyclonal antibodies?

16 A. This is a lot of different bacteria and  
17 virus, so I really don't recall.

18 Q. In what animals did you try and raise the  
19 antibody?

20 A. Mostly rabbit.

21 Q. Rabbits. Animals other than rabbits?

22 A. Sometime we use a guinea pig.

23 Q. Guinea pig. Any other animals that you can  
24 remember?

25

1 A. I don't remember.  
 2 Q. Did you use mice?  
 3 A. Rarely.  
 4 Q. Rarely. But you did use them sometimes?  
 5 A. Yes.  
 6 Q. How about rats?  
 7 A. I don't recall.  
 8 Q. Horses?  
 9 A. No.  
 10 Q. No. Did you begin work --  
 11 Did you continue working at National Taiwan  
 12 University immediately after you graduated in 1961?  
 13 A. I did my military service for one year.  
 14 Q. From 1961 to 1962?  
 15 A. Correct.  
 16 Q. Did you begin working at National Taiwan  
 17 University in 1962?  
 18 A. Correct.  
 19 Q. And when did you finish working there?  
 20 A. '67.  
 21 Q. What were your job titles while you were  
 22 working at --  
 23 A. I was instructor of microbiology and  
 24 immunology.  
 25

1 Q. Instructor in microbiology and immunology?  
 2 A. Correct.  
 3 Q. And you had that title when you --  
 4 That was still your title when you finished  
 5 working at the university?  
 6 A. Correct.  
 7 Q. What were your responsibilities while you  
 8 were working there?  
 9 A. This is two responsibility. One is research  
 10 project, and other is help to teach the student.  
 11 Medical student, dental student and so on.  
 12 Q. Tell me about your research while you were  
 13 working at National Taiwan University. This is now as  
 14 a graduate. What projects were you involved in there?  
 15 A. The big project is at that time people find  
 16 the polio vaccine is heavily contaminated with SV-40,  
 17 and the SV-40 has been proved to induce tumor in  
 18 newborn hamster.  
 19 So people worry about if people get a polio  
 20 vaccine contaminated with SV-40, eventually will get  
 21 cancer or not.  
 22 So our big project is since we cannot use a  
 23 human, can we use a primate, like a monkey, to do the  
 24 similar experiment.  
 25

1 So we grow the SV-40, we get a pregnant  
 2 mother monkey and we get a newborn monkey and try to  
 3 inject SV-40 in the newborn monkey and try to see what  
 4 kind of outcome we get.  
 5 So in order to do that, since SV-40 is the  
 6 serum virus only found in monkey, but this polio virus  
 7 also induce a tumor in newborn hamster and that is --  
 8 we used that as a control.  
 9 At the same time, we have to use other  
 10 virus, so I work not only on this virus, we also work  
 11 on polio virus.  
 12 Q. So to summarize that, would it be accurate  
 13 to say that you worked with viruses including polio  
 14 virus, SV-40, proteoma --  
 15 A. Polyoma.  
 16 Q. -- polyoma virus, injecting them into  
 17 primates, including monkeys, as well as hamsters?  
 18 A. Right. At the same time we have to develop  
 19 some tissue culture system in order to grow all these  
 20 different viruses.  
 21 Q. Okay. You described that as your big  
 22 project, your major project. Is that right?  
 23 A. That is clearly where the money come from.  
 24 Q. Did you have minor projects as well?  
 25

1 A. That is -- we have to do a lot of control.  
 2 Q. So your projects were all related to this  
 3 one?  
 4 A. Correct.  
 5 Q. What did you do immediately after you left  
 6 National Taiwan University in 1967?  
 7 A. I did my graduate work.  
 8 Q. When did you begin as a graduate --  
 9 A. '67.  
 10 Q. In 1967 at Albert Einstein College of  
 11 Medicine. When did you finish your graduate studies?  
 12 A. In '72.  
 13 Q. Did you graduate in that year?  
 14 A. Correct.  
 15 Q. What was your Ph.D. thesis about?  
 16 A. In vitro replication of RNA virus.  
 17 Q. In vitro replication of?  
 18 A. Phage RNA.  
 19 Q. Phage RNA?  
 20 A. Correct.  
 21 Q. Sometimes it happens that students start out  
 22 on one project, move to a second project, and then  
 23 finally focus on a third project.  
 24 Did you have any other projects besides the  
 25

1 one you've just told me about?  
 2 A. No. That is only project.  
 3 Q. Can you tell me a little bit more about what  
 4 that project involved?  
 5 A. We want to find a system in vitro to  
 6 replicate infectious RNA, and we use the RNA phage from  
 7 E. coli as the model system.  
 8 Q. Would you explain to me what a phage is?  
 9 A. Phage is the virus infected E. coli or  
 10 bacteria.  
 11 Q. So this phage was an RNA virus?  
 12 A. Correct.  
 13 Q. Was it a positive-stranded RNA virus?  
 14 A. In bacteria phage, we don't use the positive  
 15 strain and minor strain.  
 16 So, yes, if you can define, it have a  
 17 message, messenger property. So you can say that is  
 18 positive.  
 19 Q. Will you explain to me what is a  
 20 positive-stranded RNA virus?  
 21 A. It's similar to messenger RNA. The genome  
 22 of the cell carries the message.  
 23 Q. And if it's not positive-stranded, is it  
 24 negative-stranded?  
 25

25

26

1 A. I guess so, yes.  
 2 Q. And would you explain to me what the  
 3 difference is between them, between the  
 4 positive-stranded and the negative-stranded viruses?  
 5 A. If I remember correctly from the textbook,  
 6 the minor strain doesn't have the message, doesn't  
 7 encode the polyprotein by itself.  
 8 You have to convert it into a positive  
 9 strain in order to get that function.  
 10 Q. So a positive-stranded virus would be one  
 11 where the virus nucleic acid carries the message?  
 12 A. As I understand.  
 13 Q. Going back to your Ph.D. work at Albert  
 14 Einstein, did you use any molecular biology techniques  
 15 at that time?  
 16 A. That is -- I got my Ph.D. in molecular  
 17 biology.  
 18 Q. Ah, right. I had forgotten. Okay.  
 19 And what did you do immediately after  
 20 leaving -- graduating from Albert Einstein in 1972?  
 21 A. I did my postdoc at Yale.  
 22 Q. You began at Yale in 1972?  
 23 A. Actually a little bit earlier.  
 24 Q. In 1971?  
 25

27

1 A. '71, yeah.  
 2 Q. And when did you conclude your postdoc at  
 3 Yale?  
 4 A. '78.  
 5 Q. What was your title when you began at Yale  
 6 in '71?  
 7 A. It's postdoctoral fellow.  
 8 Q. And did your title change?  
 9 A. And then research associate.  
 10 Q. When did you become a research associate?  
 11 A. I don't recall. Maybe up to four years.  
 12 Q. About 1975?  
 13 A. Yes.  
 14 Q. And were you still a research associate  
 15 until 1978?  
 16 A. That's correct.  
 17 Q. Would you tell me what you worked on as a  
 18 postdoctoral fellow at Yale?  
 19 A. I work on the fruit fly, drosophila.  
 20 (Reporter interruption.)  
 21 MR. RABINOWITZ: Q. Is that  
 22 D-R-O-S-O-P-H-I-L-A?  
 23 A. Drosophila, yeah. I can correct that later  
 24 on.  
 25

28

1 Q. What did you do, what did you study  
2 drosophila to determine?  
3 A. Try to study the development of biology.  
4 Q. Okay. Did you work on anything else while  
5 you were there?  
6 A. In term of organism?  
7 Q. Besides looking at the developmental biology  
8 of fruit fly.  
9 A. That is very broad. So you have to define  
10 your question.  
11 Q. Did you work on a single project for the --  
12 all the time you were at Yale as a postdoc?  
13 A. Not a single one. There's several different  
14 projects. Try to understand how the fruit fly lay the  
15 egg, very simple egg, and then why from the egg it  
16 become the head, and the bottom of the side become  
17 wing, what controls that mechanism.  
18 Q. But they were all in the general area of  
19 developmental biology of drosophila?  
20 A. Yes, correct.  
21 Q. Did you use any immunology techniques --  
22 A. Yes, I did.  
23 Q. What did you do with regard to immunology  
24 while you were a postdoc?  
25

1 A. That depend how you define, so you are  
2 talking about a titre of antibody or the quality of the  
3 antibody? So that is different.  
4 So don't say in general. You have to define  
5 for me.  
6 Q. Does it sometimes happen that a particular  
7 animal doesn't make antibodies against a particular  
8 protein at all, whereas another animal does?  
9 A. I cannot recall that, no. I don't think  
10 that is true statement.  
11 Q. Well, let's take an example of porcine  
12 insulin. All right? Insulin from pigs.  
13 A. Okay.  
14 Q. If that were injected into humans, as  
15 happens in therapy, do you know whether you get  
16 antibodies, human antibodies against the pig insulin?  
17 MR. GRECO: Object to the question.  
18 You can answer. Go ahead.  
19 THE WITNESS: To your knowledge, insulin  
20 of human and the porcine only one amino acid different?  
21 MR. RABINOWITZ: Q. But do you know whether  
22 or not humans make antibodies --  
23 A. Some human will because it is one amino acid  
24 different.  
25

1 A. Try to use a polyclonal antibody to study  
2 the development of biology.  
3 Q. What did you make polyclonal antibodies  
4 against?  
5 A. Against some protein from the drosophila  
6 embryo or egg.  
7 Q. Would you just explain to me what a  
8 polyclonal antibody is? It's a term that we've used  
9 without explaining up to now.  
10 A. When you inject the antigen or immunogen  
11 into the animal, and you get a serum from animal and  
12 try to find the antibody in that serum, that more  
13 likely is a polyclonal antibody. It's a mixture of  
14 antibody.  
15 Q. When you inject a protein into an animal, do  
16 you always get antibodies against the protein?  
17 A. That is not always. That depend on what  
18 kind of protein you inject.  
19 Q. Okay. Does it matter what animal you are  
20 using to inject the protein into?  
21 A. Yes, it does.  
22 Q. So is it the case that one animal, say a  
23 rabbit, might make antibodies against a given protein  
24 and another animal, like a horse, might not?  
25

1    antibodies against a protein, you also need to know the  
 2    conditions under which the protein is administered to  
 3    the animal?

4    A.       If you are using the conserve protein.

5         So if you inject the foreign protein to  
 6    animal never sees this before, then more likely you  
 7    will make antibody.

8    Q.       Now, you mentioned whether the protein has  
 9    been denatured influences the antibody response. Is  
 10   that correct?

11   A.       That's correct.

12   Q.       What other things would influence the  
 13   antibody response?

14   A.       I think you have to rephrase the question  
 15   for me, because what you are thinking may be different  
 16   from what I'm thinking.

17   Q.       You said to me that the antibody response to  
 18   an injected protein would -- might depend on whether  
 19   the protein has been denatured; is that accurate?

20   A.       If you want to make antibody, I give you  
 21   example like actin, then you have to denature it in  
 22   order to get an antibody. So I give you this example.

23         If you want to ask me about other example,  
 24   then you have to give me the particular. Your insulin

25

1    is a good one, but give me some example, maybe I can  
 2    answer it.

3    Q.       But as a general matter, I'm trying to  
 4    elicit some general principles now --

5    A.       In science, there's no general. So you have  
 6    to --

7         You cannot generalize. There's a lot of  
 8    things you can generalize, sometimes you cannot.  
 9    There's some exception, what I try to say.

10   Q.       Okay. Would you explain to me, please, what  
 11   an epitope is?

12         MR. GRECO:      I'm going to object to this  
 13   whole line of questioning. He can answer the question;  
 14   but this is, I think, A, irrelevant to the case we're  
 15   litigating and, secondly, he's testifying here as a  
 16   fact witness.

17         You seem to be very far afield from the  
 18   issues in the case, but you go ahead and answer. I  
 19   have my objection on the record.

20         THE WITNESS:      Yes. As I understand,  
 21   epitope is the region where bind the antibody. So that  
 22   is definition.

23         MR. RABINOWITZ: Q. It's a region of?  
 24   A.       Of peptide.

25

1    Q.       So an epitope is a region of a peptide to  
 2    which an antibody binds?

3    A.       Correct.

4    Q.       Is that the same thing as an antigenic  
 5    determinant?

6    A.       Antigenic -- I would say not exactly.

7    Q.       What is an antigenic determinant?

8    A.       Antigenic determinant is the region we are  
 9    eliciting the antibody.

10   Q.       So an antigenic determinant is a region of a  
 11   peptide that elicits an antibody response?

12   A.       You can say peptide, or some other thing.

13   Q.       Of an antigen including a peptide?

14   A.       Right.

15   Q.       Whereas an epitope is a region of an  
 16   antigen, such as a peptide, to which an antibody binds?

17   A.       Right.

18   Q.       Now, if I take a peptide, would insulin,  
 19   human insulin, be an example of a peptide?

20   A.       It's a polypeptide, yes.

21   Q.       If I inject that into, say, rabbits and into  
 22   horses, would the rabbits recognize the same epitopes  
 23   as the horses would?

24   A.       No.

25

1    Q.       Why not?

2    A.       You inject into the same horses, you don't  
 3    get the same response.

4    Q.       I'm sorry, would you say that again?

5    A.       Even when you inject into the same animal,  
 6    you don't necessarily get identical result.

7    Q.       You mean into different individuals of the  
 8    same species?

9    A.       Correct.

10   Q.       So if I inject human insulin into one  
 11   rabbit, that rabbit would not in general recognize the  
 12   same epitopes as a second rabbit?

13   A.       That in general is true.

14   Q.       And that's true for horses as well?

15   A.       I guess so.

16   Q.       Would that be true for humans?

17   A.       You inject human into human?

18   Q.       No. If I inject a protein or a peptide, a  
 19   non-human protein or peptide into humans.

20   A.       That in general is true.

21   Q.       So different individuals of the same species  
 22   do not generally recognize exactly the same epitopes on  
 23   a given protein?

24   A.       That in general is correct.

25

1 Q. Is that also true when you're comparing  
2 different species of responders?

3 MR. GRECO: Same objection. Again,  
4 you're getting further and further away from anything  
5 conceivably related to this case.

6 This is an interesting academic discussion,  
7 but he's not testifying here as an expert, and I don't  
8 see what insulin in horses has anything to do with the  
9 patents we're litigating.

10 I'll let you continue for a while. Go  
11 ahead.

12 THE WITNESS: Can you ask the question  
13 again?

14 MR. RABINOWITZ: Q. Yes. You've just told  
15 me that in general different individuals from the same  
16 species do not recognize exactly the same epitopes on  
17 an injected, administered antigen.

18 Is that also true for -- if I injected into  
19 one species compared to injecting it into a different  
20 species?

21 A. Okay. So here is you want to see the  
22 different, or you want to see the similarity?

23 Q. I'm asking whether a different species, like  
24 a rabbit versus a horse, would recognize exactly the

25

1 same epitope on a protein that's foreign to both of  
2 them.

3 A. No, I try to correct my answer earlier on.  
4 If you inject into a rabbit with the same  
5 antigen, the rabbit will generally -- the antibody  
6 recognizes general epitope, but at the same time will  
7 generate different antibody.

8 So there's a different. There's a  
9 similarity, too.

10 Q. So the rabbit would recognize a variety of  
11 epitopes on the protein?

12 A. Right, unless there's some different -- or  
13 some will be different, some will be the same.

14 Q. And the horse would also recognize a variety  
15 of epitopes on the protein?

16 A. I never work with horse, but I guess that is  
17 generally true.

18 Q. But the epitopes recognized by the rabbit  
19 would not in general be the same epitopes as the  
20 epitopes recognized by the horse?

21 A. I didn't say that.

22 Q. I'm asking if that's --

23 A. That is not necessarily true.

24 Q. There might be some overlap?

25

1 A. Yes.

2 Q. Are there likely to be some differences?

3 A. That's correct.

4 Q. Okay. Let's go back to your postdoc at  
5 Yale. You said that you, as far as immunology is  
6 concerned, you were developing polyclonal antibodies  
7 against proteins from drosophila.

8 Did you have any other immunology project?

9 A. That is a very, very big project.

10 Q. I understand that, but besides that very big  
11 project, did you have other immunology projects?

12 A. No.

13 Q. What did you do immediately after leaving  
14 Yale in 1978?

15 A. I just state I also work with, try to find  
16 out the complexity for messenger RNA in the drosophila.

17 Q. Any other projects you can think of that you  
18 did while at Yale? And we're talking about in broad  
19 categories.

20 A. That's all.

21 Q. What did you do immediately after leaving  
22 Yale in 1978?

23 A. I come to UCSF School of Medicine department  
24 of biochemistry.

25

1 Q. Did you begin at UCSF in 1978?

2 A. Correct.

3 Q. When did you leave UCSF?

4 A. '81.

5 Q. What was your title when you began?

6 A. At?

7 Q. At UCSF.

8 A. Assistant research biochemist.

9 Q. And did you have the same title when you  
10 finished in 1981?

11 A. Correct.

12 Q. What did you do research-wise while you were  
13 at UCSF?

14 A. Continue very similar what I did at Yale.

15 Q. So you continued with the drosophila  
16 developmental studies?

17 A. Correct.

18 Q. Did you continue to raise polyclonal  
19 antibodies?

20 A. At that time I switched to monoclonal  
21 antibody.

22 Q. Did you continue to research the complexity  
23 of RNA in drosophila?

24 A. Correct.

1 Q. Did you work with viruses during this time?  
 2 A. No.  
 3 Q. Did you work with viruses while you were at  
 4 Yale?  
 5 A. I don't recall.  
 6 Q. What did you do immediately after leaving  
 7 UCSF in 1981?  
 8 A. I joined Chiron Corporation.  
 9 Q. Did you join Chiron in 1981?  
 10 A. Correct.  
 11 Q. What was your title in the beginning at  
 12 Chiron?  
 13 A. Senior scientist.  
 14 Q. Did that title ever change?  
 15 A. Yes.  
 16 Q. When did that change?  
 17 A. I don't recall. Changed to research --  
 18 director of research, and later on changed to Chiron  
 19 fellow.  
 20 Q. So you were a senior scientist, and then the  
 21 next title you had was director of research?  
 22 A. Correct.  
 23 Q. And after --  
 24 A. Then Chiron fellow.  
 25

1 Q. The next title you had after director of  
 2 research was Chiron fellow.  
 3 A. Correct.  
 4 Q. Do you know when you became a Chiron fellow?  
 5 A. '92.  
 6 Q. Do you know approximately how long after you  
 7 began at Chiron you were made director of research?  
 8 A. I don't recall.  
 9 Q. Was it more than five years later?  
 10 A. Four or five years, yes.  
 11 Q. Would that be 1985 to 1986?  
 12 A. That's -- yeah.  
 13 Q. When you joined Chiron in 1981, what did you  
 14 begin working with?  
 15 A. My project is the factor VIII project.  
 16 Factor VIII.  
 17 Q. What did you do with respect to factor VIII?  
 18 A. Try to purify factor VIII to identify  
 19 factor VIII peptide in order to sequence, then to clone  
 20 the factor VIII.  
 21 Q. Okay. Were there any other projects you  
 22 were working on apart from this factor VIII project?  
 23 A. Then I got involved in the hepatitis B  
 24 surface antigen project.  
 25

1 Q. Hepatitis?  
 2 A. B.  
 3 Q. B surface antigen. When did you begin  
 4 working on that project?  
 5 A. This is overlapping project.  
 6 Q. Right. So your involvement with the  
 7 factor VIII project began in 1981.  
 8 A. Right.  
 9 Q. When did your involvement with the  
 10 hepatitis B surface antigen project begin?  
 11 A. That is always we have very few people, so a  
 12 lot of people working several different project.  
 13 Q. Did the hepatitis B project begin as early  
 14 as 1981 as well?  
 15 A. Correct.  
 16 Q. Any other projects while you were a senior  
 17 scientist?  
 18 A. I think that maybe that's it.  
 19 Q. When did you stop working with factor VIII,  
 20 with the factor VIII project?  
 21 A. You mean stop or start?  
 22 Q. Stop. You began in 1981. When did that  
 23 end?  
 24 A. I could not recall. Because this is another  
 25

1 overlapping project, so it's continuous.  
 2 Q. Do you continue to work with the factor VIII  
 3 project today?  
 4 A. Right, so then we -- no, because we pass to  
 5 other people.  
 6 Once we identify the peptide, we give the  
 7 people material to sequence amino acid, once get amino  
 8 acid sequence, give to the cloner to clone the  
 9 factor VIII.  
 10 Q. Did you continue to work on the factor VIII  
 11 project after you became a director of research?  
 12 A. I don't think so.  
 13 Q. So as far as you can remember, you stopped  
 14 working on that before you became a director of  
 15 research?  
 16 A. That's right.  
 17 Q. And as for the hepatitis B surface antigen  
 18 project, did you continue working with that after you  
 19 became director of research?  
 20 A. Yes, we also involved in the hepatitis B  
 21 diagnostic project.  
 22 Q. Hepatitis B diagnostic project. When did  
 23 that begin?  
 24 A. I don't recall a time.  
 25

1 Q. Did it begin before you became a director of  
2 research?

3 A. Maybe a little bit earlier.

4 Q. And your involvement with it began around  
5 the time or a little earlier perhaps than you became  
6 director of research?

7 A. Right.

8 Q. As director of research, apart from the  
9 hepatitis B diagnostic project, what other projects  
10 were you involved in?

11 A. Involved in the Tumor Necrosis Factor, TNF.

12 Q. What were you doing with respect to Tumor  
13 Necrosis Factor?

14 A. We try to generate monoclonal antibody for  
15 the septic shock, or sepsis.

16 Q. And any other project while you were  
17 director of research?

18 A. No, that's almost it.

19 Q. So you were working on hepatitis B and Tumor  
20 Necrosis Factor factor, and nothing else as far as you  
21 can remember?

22 A. Right. At the same time, we --

23 There's only few senior scientists at  
24 Chiron, so we always have a meeting, we always discuss.

25

1 But in term of responsibilities, that maybe is my  
2 responsibility.

3 Q. In terms of your responsibility and your own  
4 research?

5 A. Correct.

6 Q. And as a Chiron fellow, what were you  
7 working on?

8 A. Right now it's hepatitis C.

9 Q. When did you begin working on hepatitis C?

10 A. That is -- now, again, your question is too  
11 broad.

12 If earlier on I start to discuss with  
13 Michael, collaborate with Michael, that is hepatitis C  
14 project or not?

15 Michael is the project leader.

16 Q. When you say "Michael," is this Michael --

17 A. Houghton.

18 Q. -- Houghton? When did you yourself begin  
19 doing experimental work on hepatitis C?

20 A. Maybe it's '85.

21 Q. While you were --

22 After you became director of research?

23 A. Yes.

24 Q. Just so that I understand correctly, you did  
25

1 not do any research yourself on hepatitis C as a senior  
2 scientist?

3 A. But my chairman ask me to do something on  
4 the non A, non B, or hepatitis C, when I joined. So  
5 that is working on?

6 Because, again, your question is too vague.  
7 I cannot really answer your question.

8 So when we have -- '81, we have a company,  
9 we set up a project. Non A, non B hepatitis is one of  
10 the project, and my chairman ask me to get involved in  
11 that. And so I try to work to develop the monoclonal  
12 antibody.

13 So is that a project, or is it involved or  
14 not?

15 Q. Did you do any experimental work with  
16 respect to -- in response to that request by your  
17 chairman?

18 A. Well, I didn't.

19 Q. You did not?

20 A. Did not.

21 Q. Okay. When -- do you recall --

22 When you say your chairman, who was that?

23 A. Dr. Rutter.

24 Q. So Dr. Rutter asked you to develop

25

1 monoclonal antibodies against non A, non B hepatitis?

2 A. Yes.

3 Q. Do you recall when that was?

4 A. In early '82.

5 Q. And you did --

6 But, however, you did not do any  
7 experimental work --

8 A. That's correct.

9 Q. -- towards that goal?

10 A. Right, but we discuss the project.

11 Q. Did you ever do any experimental work with  
12 respect to the project you're talking about now,  
13 identified by Dr. Rutter, of making monoclonal  
14 antibodies?

15 A. Right now?

16 Q. At any time while you were at Chiron.

17 A. Yes.

18 Q. When did that begin?

19 A. After we clone hepatitis C.

20 Q. Okay. When did you --

21 What year, do you recall?

22 A. You mean the time to clone hepatitis C, or

23 what --

24 Q. No, at what time did you begin working on

25

1 making monoclonal antibodies to hepatitis C.  
 2 A. After we clone the 5-1-1, we clone the  
 3 C-100. We have the antigen. We decide to make a  
 4 polyclonal antibody. Sometime we make a monoclonal  
 5 antibody.

6 Not necessarily in my lab. We can send out  
 7 to other outside to make it.

8 Q. So when did you clone hepatitis C?

9 A. So, again, we identify, or we --

10 Q. You said you cloned hepatitis C. Is that  
 11 right?

12 A. Our group.

13 Q. Yes, your group cloned hepatitis C.

14 A. Yeah, so after we clone 5-1-1.

15 Q. When did that happen?

16 A. It is '87 we really identify.

17 Q. So did you yourself or anyone that you were  
 18 directly supervising begin working to make monoclonal  
 19 antibodies to hepatitis C proteins after 1987?

20 A. You mean after or before?

21 Q. After. I thought you told me --

22 Is it correct that you and the people who  
 23 were working under you did not attempt to make  
 24 monoclonal antibodies before 5-1-1 was cloned?

25

1 A. Because we don't have antigen.  
 2 Q. Is that correct, is that accurate, that you  
 3 did not?

4 A. No, that's correct. But for my group, but I  
 5 didn't say the other group at Chiron.

6 Q. Okay. But your group did not attempt to  
 7 make monoclonal antibodies --

8 A. That's correct.

9 Q. -- against non A, non B hepatitis until  
 10 after 5-1-1 was cloned. Right?

11 A. That's correct.

12 Q. You mentioned another group that was --  
 13 Was there a group that did try and do that?

14 A. I guess so, but you better ask Michael  
 15 Houghton.

16 Q. I see. So you don't know whether or not  
 17 Dr. Houghton's group was attempting to make antibodies?

18 A. I believe they try.

19 Q. Do you know whether they succeeded at that  
 20 time?

21 A. You have to ask Michael.

22 When you say "succeeded," so that is also  
 23 you have to define for me. "Succeed" mean a lot of  
 24 different things.

25

1 I do believe they succeed to generate  
 2 monoclonal antibody, but they have no way to know they  
 3 have antibody. So are you going to say they succeed or  
 4 they fail?

5 MR. RABINOWITZ: Okay. I think that's a  
 6 very specific answer, which satisfies me to that  
 7 question.

8 Would this be a good time for a break?

9 MR. GRECO: If you'd like, sure.

10 THE VIDEOGRAPHER: Going off record. Time  
 11 now is 10:01.

12 (Recess.)

13 THE VIDEOGRAPHER: Going back on record.

14 Time now is 10:12.

15 MR. RABINOWITZ: Q. Dr. Kuo, let me take  
 16 you back to when you began at Chiron as a senior  
 17 scientist in 1981. Whom did you report to at that  
 18 time?

19 A. Dr. Pablo Valenzuela.

20 Q. Can you spell his name?

21 A. Pablo.

22 Q. Pablo?

23 A. Valenzuela, V-A-L-E-N-Z-U-E-L-A.

24 Q. Was he your direct supervisor?

25

1 A. He's a research director.

2 Q. And did you work in a group with other  
 3 scientists?

4 A. Yes.

5 Q. Who else was working in your group at the  
 6 time?

7 A. Brian Craine, C-R-A-I-N-E.

8 Q. C-R-E-I?

9 A. A-I-N-E.

10 Q. Anyone else?

11 A. That's it. He's a Ph.D. scientist.

12 Q. Other scientists without Ph.D.s?

13 A. We call research associate.

14 Q. Okay. Were there research associates in  
 15 your group?

16 A. Yes.

17 Q. Who were they?

18 A. It's Won Sang Lee, L-E-E, and Carol Kuo.

19 Q. K-U-O, the same as the spelling of your  
 20 name?

21 A. Yes.

22 Q. Besides Won Sang Lee and Carol Kuo, who  
 23 else?

24 A. We are very small group. We work very

25

1 closely, so you have to define.

2 Like factor VIII project, I am in charge of  
 3 purify factor VIII. Someone else is going to sequence  
 4 it. Someone else is going to do the cloning. So they  
 5 are all factor VIII team.

6 Q. But was there a formal group to which you  
 7 were assigned for organizational purposes?

8 A. We didn't have -- everybody individual.

9 Q. I see.

10 A. At that time, everybody report to Pablo  
 11 Valenzuela. So we run like a university.

12 Q. Whom were you working with on the  
 13 hepatitis B surface antigen project?

14 A. That is Pablo Valenzuela's project.

15 Q. What other scientists were you working with  
 16 on that project?

17 A. I just say, it's very early on. We,  
 18 everybody, get involved.

19 Q. So you were working with Brian Craine on  
 20 that project?

21 A. Yes.

22 Q. Were you working with any other scientists  
 23 on that project besides Brian Craine?

24 When I say "scientists," I'm using it in the

25

1 sense that you used it, people with Ph.D.'s.

2 A. So with Pablo and with other people.

3 Q. What other people?

4 A. You have to go back to all very early on  
 5 Chiron. Everybody involved. So you have to define.

6 I think it's difficult for me. If you name  
 7 the someone, then I can answer yes, he's involved. But  
 8 if you ask from the top of my head, I cannot answer.

9 Q. Are you saying that every single Ph.D.  
 10 scientist at Chiron was involved in the hepatitis B  
 11 surface antigen --

12 A. Very early on, everybody get involved.

13 Q. How many Ph.D. scientists were there at  
 14 Chiron?

15 A. There may be only less than 20.

16 Q. And is it your testimony that all 20 of  
 17 those were working on the hepatitis B surface antigen  
 18 project?

19 A. Involved in it.

20 Q. Well, can you name some of them for me to  
 21 the best of your recollection?

22 A. Like Graham Bell, Robert Hallowell.

23 Q. Can you spell that?

24 A. Maybe later on I can spell for you.

25

1 Q. Is that H-A-L-I-W-E-L-L?

2 A. Something like that, but I don't remember.

3 Q. Any more names you can remember of Ph.D.'s  
 4 who were working on --

5 A. Martha Truett. Frank Majors (phonetic).

6 That's all I can remember.

7 Q. Those are all you remember?

8 A. Yes.

9 Q. Now, with respect to the hepatitis B  
 10 diagnostic project, whom did you report to for that?

11 A. Still is Pablo Valenzuela.

12 Q. Were the Ph.D.s working with you on that  
 13 project the same as the Ph.D.s who were working with  
 14 you on the surface antigen project?

15 A. Actually, this is a contract research  
 16 project with Lucky Goldstar, Korean company.

17 Q. Yes?

18 A. They send a lot of scientists to my lab.

19 Q. Can you tell me --

20 A. At the same time, Pablo Valenzuela and his  
 21 people are also involved in this.

22 Q. So as far as the Chiron people were  
 23 concerned, were they the same people as were working on  
 24 the hepatitis B surface antigen project?

25

1 A. That's correct, and plus the people report  
 2 directly to Pablo. His own group.

3 Q. And in addition, were there people from --

4 sent by Goldstar who were working on the diagnostic

5 project?

6 A. Yes, the same involvement.

7 Q. And can you tell me their names?

8 A. I'm sorry, I don't recall that.

9 Q. You don't remember the names of any of the

10 Goldstar scientists?

11 A. This, I don't remember. If you give me some  
 12 time, I can write it down.

13 Q. Okay, that's fine. As I said to you at the  
 14 beginning, Dr. Kuo, if you recall in the course of the

15 deposition more names in response to this, just let us  
 16 know and we'll give you an opportunity to mention them.

17 A. Sure.

18 Q. When you say hepatitis B diagnostic project,  
 19 what did that project involve?

20 A. Involved develop the diagnostic test for

21 hepatitis B surface antigen, it's anti-core, anti-e for

22 Korean market.

23 Q. Were these serological tests?

24 A. Correct. But, again, you have to say

1 surface antigen is not for serological test.  
 2 Q. What test is the surface antigen test?  
 3 A. You pick up the antigen test.  
 4 Q. By means of an antibody?  
 5 A. Yes.  
 6 Q. When you were a senior scientist, how did  
 7 you report to Dr. Valenzuela? Was that in written  
 8 form?  
 9 A. No.  
 10 Q. Did you report to him personally?  
 11 A. If necessary.  
 12 Q. Did you make regular reports to him?  
 13 A. No. We are individual. We have 100% of  
 14 freedom to do our research.  
 15 Q. So you didn't make regular oral reports to  
 16 him or regular written reports to him?  
 17 A. No.  
 18 Q. Did you report any of your results at  
 19 meetings, laboratory meetings?  
 20 A. Very early on, we don't have regular  
 21 meeting.  
 22 Q. Did you have meetings sometimes?  
 23 A. Yes. Like we have senior scientists  
 24 meeting.  
 25

1 Q. How often would those occur?  
 2 A. Once in two months.  
 3 Q. More or less regularly once every two  
 4 months?  
 5 A. No.  
 6 Q. How many a year would you say actually  
 7 happened?  
 8 A. Five or six times.  
 9 Q. What would be discussed at senior scientist  
 10 meetings?  
 11 A. This project, direction of the research.  
 12 Q. Would each senior scientist at that meeting  
 13 describe the direction of his or her research?  
 14 A. Yes.  
 15 Q. Would they describe their recent results?  
 16 A. If they're important result.  
 17 Q. Would they give an idea of progress in their  
 18 research projects?  
 19 A. I guess so. Yes.  
 20 Q. Were minutes kept of the senior scientist  
 21 meeting?  
 22 A. I don't know.  
 23 Q. Did you ever receive a copy of any minutes  
 24 of a senior scientist --  
 25

1 A. I don't recall.  
 2 Q. Did you ever write any kind of written  
 3 report at all as a senior scientist on your research?  
 4 A. In any project?  
 5 Q. In any of the projects you were doing --  
 6 A. The factor VIII project, we would write  
 7 partially because there were so many people were  
 8 involved.  
 9 Q. Whom did you report to for the factor VIII  
 10 project?  
 11 A. Still Pablo Valenzuela.  
 12 But the project, we worked for Nordisk.  
 13 Danish company.  
 14 Q. Okay. And were written reports made in the  
 15 factor VIII project?  
 16 A. Yes, I think so.  
 17 Q. How often were they made?  
 18 A. That, I don't recall.  
 19 Q. On a regular basis?  
 20 A. "Regular" means? So you have to define.  
 21 "Regular" means once a year or six months?  
 22 Q. Do you recall it was more than once a year?  
 23 A. I think it's maybe twice a year.  
 24 Q. Did you receive copies of those reports?  
 25

1 A. Yes.  
 2 Q. Would they have been circulated to everyone  
 3 at Chiron, or only to some people at Chiron?  
 4 A. I would say so, yes.  
 5 Q. Do you think everyone got them?  
 6 A. Not everyone get it. People involved in the  
 7 factor VIII.  
 8 Q. Okay. So all the scientists working on the  
 9 project would have received --  
 10 A. Yes.  
 11 Q. When you became director of research, whom  
 12 did you report to then?  
 13 A. It's Pablo Valenzuela.  
 14 Q. What was Dr. Valenzuela's title in 1981?  
 15 A. He's vice-president and director of  
 16 research.  
 17 Q. Was that still his title in 1985 to 1986  
 18 when you became director of research?  
 19 A. Yes.  
 20 Q. Did you make -- as a director of research,  
 21 did you make written reports to anyone?  
 22 A. No. That is just the title. Still we do  
 23 the same thing.  
 24 Q. Your reporting structures didn't change when  
 25

1 you became director of research?  
 2 A. That's correct.  
 3 Q. Did you continue to attend the senior  
 4 scientist meetings when you became director of  
 5 research?  
 6 A. Then we didn't have a senior scientist  
 7 meeting. Because everybody became -- title getting  
 8 higher, so we have a Tuesday meeting. Tuesday  
 9 seminar -- weekly meeting.  
 10 Q. When did those meetings begin?  
 11 A. I don't recall.  
 12 Q. Did they begin before you became a director  
 13 of research?  
 14 A. I guess it will be around that period.  
 15 Q. What was the -- what was discussed at the  
 16 Tuesday meetings?  
 17 A. Discuss our project.  
 18 Q. Was each meeting devoted to one project, or  
 19 did everyone in turn --  
 20 A. Devoted to one project.  
 21 Q. Would you know before attending the meeting  
 22 what project would be discussed that week?  
 23 A. Yes.  
 24 Q. How did you know that?  
 25

1 A. It's announcement.  
 2 Q. In what form was the announcement made?  
 3 A. Sometime we have a memo sent out say, okay,  
 4 this week we will discuss this project; next week, all  
 5 like that.  
 6 Q. A memo that was circulated --  
 7 A. That's correct.  
 8 Q. -- at Chiron? Who circulated the memos?  
 9 A. Pablo Valenzuela will send out.  
 10 Q. Was this Tuesday meeting limited to people  
 11 working under Dr. Valenzuela, or did other people not  
 12 under him also report there, their work, at those  
 13 meetings?  
 14 A. Anybody at Chiron will attend if they want.  
 15 So it's Chiron confidential.  
 16 Q. So anyone at Chiron could attend. Does that  
 17 mean that the memos announcing the topics would be sent  
 18 to Chiron broadly and not only to Dr. Valenzuela's  
 19 group?  
 20 A. I think you have to appreciate, that is very  
 21 small company. 80%, 90% of people are working on  
 22 research.  
 23 Q. Did all the research scientists fall under  
 24 Dr. Valenzuela?  
 25

1 A. Yes.  
 2 Q. I see. So did the hepatitis -- or the  
 3 non A, non B hepatitis project fall under  
 4 Dr. Valenzuela as well?  
 5 A. That's correct.  
 6 Q. So at those Tuesday meetings, did people  
 7 report from time to time progress on the non A, non B  
 8 hepatitis project?  
 9 A. Yes.  
 10 Q. Before you became a Chiron fellow, did you  
 11 ever write written reports on your work?  
 12 A. Yes.  
 13 Q. How many times a year would you do that?  
 14 A. Only few times.  
 15 Q. A few times every year?  
 16 A. Right. But we had to write annual report.  
 17 Q. An annual report, and that accounts for one  
 18 time every year. What about the other times?  
 19 A. Just as necessary. For example, we have to  
 20 write a report to our Nordisk or Lucky Goldstar. Our  
 21 contract research, we have to write a report.  
 22 Q. Right. For projects where you didn't have  
 23 an outside collaborator, was it only the annual report  
 24 that you would write?  
 25

1 A. That's correct.  
 2 Q. Who would receive annual reports from you?  
 3 A. It's Valenzuela.  
 4 Q. Would they be circulated to anyone else?  
 5 A. No. It's confidential. It's evaluation of  
 6 your performance.  
 7 Q. Did Dr. Valenzuela alone evaluate you?  
 8 A. That, I don't know.  
 9 Q. So you don't know whether he -- whether  
 10 those reports were shown to other people who were --  
 11 who may have been involved in evaluating?  
 12 A. I don't know.  
 13 Q. While you were a director of research, did  
 14 you include work on the non A, non B hepatitis project  
 15 in any of your annual reports?  
 16 A. Yes.  
 17 Q. Do you remember the first year in which you  
 18 included such work in an annual report?  
 19 A. No, no. We are confused here.  
 20 Annual report is just performance report.  
 21 It's not what you are thinking about, annual report.  
 22 It's what did you do for this year.  
 23 So if for this year I write down, I say I  
 24 did TNF, I did non A, non B or hepatitis C project, I  
 25

1 would just write down. It's not like a report.  
 2 Q. So it included experimental -- it included  
 3 work that you did?  
 4 A. Yes. No experimental detail.  
 5 Q. And you did write annual reports which  
 6 included information about your involvement on the  
 7 non A, non B hepatitis project; correct?  
 8 A. That's correct.  
 9 Q. When was the first year in which your annual  
 10 report included subject matter concerning the non A,  
 11 non B hepatitis project?  
 12 A. So we are confused here.  
 13 You ask me, in general do you write annual  
 14 report. I say this is for the performance, we have to  
 15 write for Pablo Valenzuela or human resources. And you  
 16 try to ask me when. The time, I don't recall.  
 17 But we do have a non A, non B hepatitis  
 18 project report, so we will be edited by Michael  
 19 Houghton.  
 20 So among those report, I will have to write  
 21 small part or big part of it. That depend on how much  
 22 we did in my group.  
 23 Q. So apart from your annual reports, you also  
 24 prepared reports to Dr. Houghton for him to --  
 25

1 A. No.  
 2 Q. '86?  
 3 A. '85-'86, maybe.  
 4 Q. Are you saying '85 no, '86 maybe?  
 5 A. No. The report you are --  
 6 Your question make me very difficult to  
 7 answer.  
 8 Q. Okay. Let's try it this way.  
 9 A. So you are trying to say written report, or  
 10 are you trying to say did you involve in the non A,  
 11 non B hepatitis research, or discuss with that. That  
 12 is different.  
 13 Q. I'm asking now about written reports. I'm  
 14 asking --  
 15 I'm trying to work with you to establish the  
 16 first year in which you produced a written report to  
 17 send to Dr. Houghton concerning the non A, non B  
 18 hepatitis project. So far you recall that you didn't  
 19 do it up to 1984.  
 20 A. All right.  
 21 Q. And I'm now asking, do you recall whether  
 22 you wrote such a report in 1985?  
 23 A. But as you know, I didn't report to Michael  
 24 Houghton. I only report to Pablo Valenzuela, so  
 25

1 A. To edit.  
 2 Q. -- to edit for purposes of producing a  
 3 non A, non B hepatitis report?  
 4 A. That's correct.  
 5 Q. How often did you send reports to  
 6 Dr. Houghton concerning the non A, non B hepatitis  
 7 project?  
 8 A. It's no regular basis.  
 9 Q. I beg your pardon?  
 10 A. There's no regular basis. When necessary,  
 11 we write.  
 12 Q. Did you not make at least an annual report  
 13 about work on the non A, non B hepatitis project to  
 14 Dr. Houghton?  
 15 A. No.  
 16 Q. Were there some years in which you never  
 17 wrote any report to Dr. Houghton?  
 18 A. Some year in '81, I didn't write. '82, I  
 19 didn't write. So --  
 20 Q. What about '83?  
 21 A. No.  
 22 Q. What about '84?  
 23 A. No.  
 24 Q. '85?  
 25

1 there's no reason I'd write a report to Michael  
 2 Houghton.  
 3 Q. Dr. Kuo, you had testified that you produced  
 4 written reports to send to Dr. Houghton so that he  
 5 could edit them and produce a non A, non B --  
 6 A. If he ask me to put together in order for  
 7 him to report to someone, I would do that.  
 8 So there's no regular basis I have to write  
 9 something to him, because I didn't report to him.  
 10 Q. Now, the reports of that kind that you've  
 11 just mentioned, did you write such a report in 1985 as  
 12 far as you can recall?  
 13 MR. GRECO: Object to the form.  
 14 THE WITNESS: I don't recall.  
 15 MR. RABINOWITZ: Q. Did you write the  
 16 report to Dr. Houghton about non A, non B hepatitis  
 17 project in 1986?  
 18 A. Written report you're talking about?  
 19 Q. A written report.  
 20 MR. GRECO: Well, object to the form.  
 21 By "report to Dr. Houghton," do you mean to  
 22 include something he wrote for Dr. Houghton to put into  
 23 some report? Is that what you mean?  
 24 MR. RABINOWITZ: Let me rephrase.  
 25

1 MR. GRECO: I think that's his  
2 confusion.

3 MR. RABINOWITZ: Let me rephrase the  
4 question.

5 Q. Did you prepare any written material and  
6 send it -- for sending to Dr. Houghton concerning the  
7 non A, non B hepatitis project in 1986?

8 A. I don't recall.

9 Q. And in 1985?

10 A. That, I don't recall.

11 Q. Do you recall with respect to 1987?

12 A. Yes.

13 Q. Did you prepare written material and send it  
14 to Dr. Houghton concerning the non A, non B hepatitis  
15 work?

16 A. I think so.

17 Q. 1988?

18 A. Yes.

19 Q. And if I ask about the years subsequent to  
20 1988, would you have done that every year until a  
21 certain time?

22 A. I would say so, yes.

23 Q. When did that stop?

24 A. We never stopped.

25

1 Q. It continues to this day?

2 A. Yes.

3 Q. Okay. So just to summarize, you recall that  
4 you wrote material to Dr. Houghton -- for Dr. Houghton  
5 to compile a project report concerning the non A, non B  
6 hepatitis project from 1987 and every year  
7 subsequently. Is that correct?

8 MR. GRECO: Object to the form.

9 THE WITNESS: As I recall.

10 MR. RABINOWITZ: Q. But you're uncertain  
11 whether you did in 1985 and 1986?

12 A. I don't recall.

13 Q. Do you know if copies of those -- of any of  
14 your written reports exist today?

15 A. That, I don't know.

16 Q. Do you keep copies of your own reports?

17 A. No.

18 Q. So you have no copies of any annual report  
19 that you wrote?

20 A. I don't think so.

21 Q. You have no copies of any written material  
22 you prepared for Dr. Houghton concerning the non A,  
23 non B hepatitis project?

24 A. We just move to the new building. We threw  
25

1 away everything.

2 Q. When did that move happen?

3 A. Last year.

4 Q. When last year?

5 A. In July.

6 Q. Do you know whether there were any copies of  
7 your annual reports in your possession before you  
8 moved?

9 A. I didn't know.

10 Q. Do you know --

11 A. Because we moved from big office to small  
12 office, so we have to get rid of a lot of different  
13 paper.

14 Q. Did you review the papers before you  
15 decided -- before some of them were discarded?

16 A. Usually, I don't.

17 Q. Did anyone review them?

18 A. No.

19 Q. How many directors of research were there at  
20 Chiron when you became a director of research?

21 A. I don't know. I don't recall. Quite a few.

22 Q. More than 50?

23 A. Less than that. Maybe five or six.

24 Q. Five or six. Can you remember any of their  
25

1 names?

2 A. Kathy Steimer, Nadine Berg (phonetic).  
3 Any other, I don't remember.

4 Q. Were there any other directors of research  
5 working with the Chiron project? Working with the -- I  
6 beg your pardon, working with the non A, non B  
7 hepatitis project?

8 A. You better ask Michael Houghton about this.  
9 He's the project leader.

10 Q. As far as you can recall, do you know  
11 whether any of the people working on the non A, non B  
12 hepatitis project had the title of director of  
13 research?

14 MR. GRECO: At any time, or when?

15 MR. RABINOWITZ: At any time.

16 THE WITNESS: I don't remember. I think  
17 you better ask Michael Houghton. I really don't know.

18 MR. RABINOWITZ: Okay.

19 Q. So you don't know whether or not.

20 And then let me ask as a Chiron fellow, whom  
21 do you report to?

22 A. Pablo Valenzuela.

23 Q. What is Dr. Valenzuela's title today?

24 A. Senior vice-president. But this report  
25

1 system is for convenience.

2 Q. Pardon?

3 A. Chiron is for convenience. Chiron fellow is  
4 a very honorary title. It is a corporate  
5 vice-president label, so theoretically we only report  
6 to the corporation.

7 Q. So you are a vice-president of Chiron  
8 Corporation?

9 A. No. The title is fairly equal to the  
10 corporate vice-president.

11 (Reporter interruption.)

12 MR. GRECO: I think he said a fellow is  
13 equal to a corporate vice-president. Is that right?

14 THE WITNESS: Yes.

15 MR. RABINOWITZ: Q. But you are not  
16 formally a vice-president of Chiron, are you?

17 A. No.

18 Q. Do you make written reports today -- or  
19 since you have been a Chiron fellow, have you continued  
20 to make written reports?

21 A. Only for the annual evaluation.

22 Q. You continue to write an annual report for  
23 your evaluation.

24 A. Right.

25

1 Q. And whom do you send that to?

2 A. To human resources.

3 Q. To anyone -- to any named person at human  
4 resources?

5 A. To the person in charge our division.

6 Q. Who is that?

7 A. Right now, we don't have any. Just left.

8 Q. When was the last annual report that you  
9 wrote?

10 A. To whom, or?

11 Q. No, when did you write the last annual  
12 report that you wrote.

13 A. This is last year.

14 Q. And to whom did you send that report?

15 A. J. Mike Smith.

16 Q. I'm sorry, can you say that name again?

17 A. Mike Smith.

18 Q. Let me just clear up some confusion. At  
19 some point did you send annual reports to  
20 Dr. Valenzuela?

21 A. Yes.

22 Q. Did you also send copies of those reports to  
23 human resources?

24 A. At that time we did not have human

25

1 resources.

2 Q. I see. When did you first have a human  
3 resources department?

4 A. I don't recall.

5 Q. Does Dr. Valenzuela continue --  
6 Since you've had a human resources  
7 department, does Dr. Valenzuela continue to receive  
8 copies of your annual report as well?

9 A. Yes. He has to sign before he send out.

10 Q. Dr. Kuo, you mentioned that as a Chiron  
11 fellow you have the same rank as a corporate  
12 vice-president. Do you own stock in Chiron?

13 A. Yes, I do.

14 Q. Do you have options to purchase stock in  
15 Chiron?

16 A. Yes.

17 Q. Do you have any financial interest in the  
18 litigation between Chiron and Roche?

19 MR. GRECO: Object to the form.

20 THE WITNESS: Yes.

21 MR. RABINOWITZ: Q. Can you answer the  
22 question, please?

23 A. Define "financial interests"? If I own the  
24 Chiron, that is a financial interest? If the Chiron

1 stock go up? That is also --

2 Q. Let me clarify. Apart from your ownership  
3 of Chiron stock and Chiron stock options, other than  
4 that, do you have any financial interest in the  
5 litigation between Chiron and Roche?

6 A. No, I don't.

7 Q. Do you receive any revenue from royalties  
8 paid under the Chiron patents directed to HCV?

9 A. I get one dollar out of the patent. Is that  
10 revenue or not?

11 Q. Apart from that one dollar, do you receive  
12 any other moneys from royalties paid under those  
13 patents?

14 A. No, I don't.

15 Q. Did Chiron pay you the dollar?

16 A. Yes, they did.

17 Q. With a bank note?

18 A. No, it's really very old one dollar bill.

19 Q. Do you still have that bill?

20 A. I don't remember. Maybe, if I look. I  
21 don't know.

22 Q. Dr. Kuo, let me ask you now about some  
23 scientific terms, and I'm going to ask you to explain  
24 to me how scientists generally use these terms in the

25

1 scientific literature. This is not in relation to any  
2 particular patents.

3 Are you familiar with the term "viral  
4 agent"?

5 A. Yes.

6 Q. What does the term "viral agent" mean as  
7 scientists use it in the scientific literature?

8 MR. GRECO: You can answer.

9 I'm going to object, just so I don't keep  
10 interrupting you, to the general definitions of terms  
11 unrelated to the patent as beyond the scope of proper  
12 examination.

13 You may go ahead and answer.

14 THE WITNESS: Maybe you refer to the  
15 virus?

16 MR. RABINOWITZ: Q. I beg your pardon?

17 A. You're talking about viral agent.

18 Q. Yes. How do scientists generally use  
19 that term?

20 A. It's a virus, or similar to a virus.

21 Or is something you don't know what kind of  
22 virus it is, so it's a very general term.

23 Q. So let me just be sure I understand your  
24 answer correctly. A viral agent refers to any virus?

25

1 MR. GRECO: Object to the form.  
2 Go ahead.

3 THE WITNESS: Yes, from my point of view,  
4 yes. You are asking my question -- you ask question to  
5 me, so my answer will be my opinion. Not general.

6 I don't speak for Michael Houghton or  
7 Qui-Lim Choo.

8 MR. RABINOWITZ: Q. I'm asking about how  
9 you understand that term.

10 A. Yes.

11 Q. So you understand the term "viral agent" in  
12 the scientific literature to refer to viruses in

13 general?

14 MR. GRECO: Object to the form.

15 THE WITNESS: I think that is correct.

16 MR. RABINOWITZ: Q. So is it true that a  
17 virus can be a viral agent even if it doesn't infect  
18 humans?

19 A. That, I could not answer because I don't  
20 know if that is true or not. From my knowledge, I  
21 cannot answer.

22 Q. Well, you've just told me that viral agent  
23 refers to viruses in general.

24 A. But that is the operation definition.

25

1 So you are working in the medical field, you  
2 are more interested in the disease. So when people  
3 mention about viral agent, more likely is some agent  
4 cause disease.

5 So we are study human biomedical field here.  
6 We are not study like RNF phage or something. So viral  
7 agent more likely in medical field more likely refer to  
8 the virus cause disease.

9 Q. And scientists who work with phages, do they  
10 use the term "viral agent" to --

11 A. I don't think so.

12 Q. What about scientists working with animal  
13 diseases, do they use the term "viral agent" --

14 A. I would say yes.

15 Q. Let me just complete my question, if you  
16 don't mind.

17 Do scientists who work with animal diseases  
18 use the word "viral agent" to include viruses infecting  
19 only animals, not humans?

20 A. That, I don't know. I'm not in that field,  
21 so I don't know.

22 Q. Have you ever seen the term "viral agent" in  
23 the literature used to refer to a virus other than a  
24 human virus?

25

1 A. I don't read those magazines in general, so  
2 I don't know.

3 Q. Let me ask you about the term "hybridize,"  
4 as applied to nucleic acids hybridizing. What does  
5 that mean?

6 A. That means it's the two strand on nucleic  
7 acid. They have a homology, so they tend to come  
8 together.

9 Q. How does that happen? What is the  
10 mechanism?

11 A. Through hydrogen bonding.

12 Q. Does that require that the sequences be  
13 complementary?

14 A. Some sequence should be complementary.

15 Q. When you say "some sequence," what do you  
16 mean?

17 A. Yes, it depend on what kind of condition you  
18 are doing hybridization. Condition is a stringent or  
19 non-stringent. So it's operational.

20 Q. So what are stringent conditions?

21 A. In the high-ionic strain or low-ionic  
22 strain?

23 Q. Okay. Under stringent conditions, are you  
24 saying that they must be completely complementary?

1 A. Not necessarily completely.  
 2 This hybridization, so you are using very,  
 3 very long term. So give me how many nucleotide we are  
 4 talking about here so I can explain to you.  
 5 Q. Oh, does it matter how many -- how long the  
 6 nucleotide sequence is?

7 A. Of course it does matter.

8 Q. What difference does that make?

9 A. Well, that depend on how you're going to run  
 10 the assay.

11 Q. So for a sequence of, say, 10 nucleotides,  
 12 what is the difference between a sequence of 10  
 13 nucleotides and a sequence of, say, 13 nucleotides?

14 MR. GRECO: Object to the form.

15 THE WITNESS: If you run 10, the  
 16 stability will be lower than the 13, in term of the  
 17 hybrid.

18 MR. RABINOWITZ: Q. So are you saying that  
 19 a sequence of 10 needs to be -- needs to have more  
 20 perfect complementarity in order to --

21 A. No, I didn't say that. I said the stability  
 22 of the hybrid will be less stable than the 13.

23 Q. Are hybrids more stable if they have better  
 24 complementarity than if they have less complementarity?

25

1 A. That is true.  
 2 Q. And if conditions are made more stringent,  
 3 does that --  
 4 Under stringent conditions, does that permit  
 5 only -- does that make -- impose a requirement for  
 6 greater complementarity to remain stable than under  
 7 less stringent conditions?

8 A. In general, that is true.

9 Q. So would you agree that hybridization means  
 10 binding of one nucleic acid sequence to another through  
 11 the binding of complementary base pairs?

12 A. Binding? No, I will say that is --  
 13 (Reporter interruption.)

14 THE WITNESS: -- hydrogen binding between  
 15 the two different strain.

16 (Reporter interruption.)

17 MR. RABINOWITZ: Q. So let me run this by  
 18 you again. I'm going to propose this as a definition  
 19 of hybridization and see whether you agree with it; or  
 20 if you don't agree with it, tell me what's wrong with  
 21 it.

22 Hybridization is binding of one nucleic acid  
 23 sequence to another through the binding of  
 24 complementary based pairs.

25

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1 A. Through hydrogen bonding.  
 2 Q. Through hydrogen binding.  
 3 MR. GRECO: "Bonding," I think he said.  
 4 THE WITNESS: Bonding.  
 5 MR. GRECO: Binding or bonding?  
 6 THE WITNESS: Bonding  
 7 MR. GRECO: Bonding.  
 8 MR. RABINOWITZ: Through hydrogen bonding.  
 9 THE WITNESS: Yes.  
 10 MR. RABINOWITZ: Q. Must the base pairs be  
 11 completely complementary?

12 A. No.

13 Q. They need not be completely complementary?  
 14 A. You can make it not completely  
 15 complementary, still there's a hybrid.

16 Q. And you say that the conditions are  
 17 important as well?

18 A. Right.

19 Q. Is there such a thing as nonspecific  
 20 hybridization?

21 MR. GRECO: Object to the form.

22 THE WITNESS: That is how you define  
 23 nonspecific.

24 MR. RABINOWITZ: Q. What do you understand

25

1 by "nonspecific hybridization"?

2 A. As you know, in any test there is no  
 3 absolute.

4 Q. Right.

5 A. For example, like immunoassay, there is  
 6 sensitivity, specificity. You want to increase the  
 7 sensitivity, the specificity is become lousy. But you  
 8 don't say there's no interaction. Right? So you have  
 9 to define certain condition for me to answer.

10 Q. I'm sorry, are you saying that nonspecific  
 11 hybridization can occur depending on the conditions of  
 12 the assay?

13 A. Yes. More likely, yes.

14 Q. What sort of things permit nonspecific  
 15 hybridization to occur?

16 A. Well, in the immunoassay or in the nucleic  
 17 acid?

18 Q. No, in the hybridization of nucleic acid.

19 A. Because I'm not the expert in nucleic acid,  
 20 so you ask me, I only can answer how much I know.

21 Q. To the best of your knowledge, what sort of  
 22 conditions permit nonspecific hybridization to occur?

23 A. It's the stringency of the hybridization.

24 Q. And so at low stringency --

25

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1 A. This tend to have more nonspecific  
2 hybridization.  
3 Q. And how do you -- how can you tell whether  
4 hybridization is specific or nonspecific?  
5 A. No, you have to confirm it.  
6 Q. How do you confirm that?  
7 A. Use alternative assay.  
8 Q. What alternative assay?  
9 A. That, you are asking me even the assay  
10 field. If you run the ELISA, you score a positive,  
11 then you have to confirm by another assay which is as  
12 sensitive and to confirm your assay is specific.  
13 Q. With respect to hybridization of  
14 nucleotides, how can you tell whether hybridization  
15 that's observed is specific or nonspecific?  
16 A. As I mentioned, I'm no expert, so I cannot  
17 answer that.  
18 Q. You don't know that.  
19 When you're dealing with -- you mentioned  
20 every assay has a background. When you're evaluating  
21 results in, let's say, serological assays --  
22 A. Right.  
23 Q. -- how do you tell whether a result you're  
24 seeing represents background or represents a specific  
25

1 yes, this is a positive.  
2 Q. So when you're looking at a result to see  
3 whether it's to be scored as positive or negative, for  
4 example, if you have radioactive counts, do you look  
5 for zero counts being negative and any counts above  
6 zero being positive?  
7 A. No, you cannot do that, but we are talking  
8 about nobody use RIA now.  
9 Q. Let's talk about an RIA for the moment.  
10 RIA, does that stand for radioimmunoassay?  
11 A. That's correct.  
12 Q. You say that a negative result need not be  
13 zero.  
14 A. Define the question for me. So where are we  
15 going, so that maybe I can answer the question.  
16 Because we don't use RIA in blood bank setting.  
17 Q. I'm talking about assays in general, I'm not  
18 talking about blood banks in particular. I'm asking  
19 you --  
20 We're talking about scoring the result as  
21 positive or negative, and I asked you whether a result  
22 must be zero in order to be scored as negative.  
23 MR. GRECO: Object to the form.  
24 THE WITNESS: That is not true, because  
25

1 binding?  
2 A. That's what I just mention. You need an  
3 alternative assay.  
4 Q. Do you ever subtract out the background?  
5 A. In a blood bank setting, usually you don't,  
6 because you don't want to make a risk. Even  
7 nonspecific or false positive, you still consider that  
8 is a positive. Because if you transfuse the blood into  
9 the recipient, it cause some disease, who is going to  
10 be responsible?  
11 Q. So you never subtract background --  
12 A. No.  
13 Q. -- from the counts at all?  
14 A. I think we are talking about two different  
15 things here.  
16 I think in the blood screening tests, even  
17 there's a false positive, unless they can confirm it is  
18 really a false positive, they can assume that is a  
19 positive.  
20 Q. Okay. When you say "a positive," do you --  
21 what do you mean?  
22 A. That means -- all the tests is licensed by  
23 FDA. So FDA will already approve your test. So all  
24 the tests when you score as a positive, then you say,  
25

1 certain result, a certain number -- a certain result  
 2 will be background, and then you have to work out how  
 3 many standard deviations above background the cutoff  
 4 will be. Is that right?

5 A. That's correct.

6 Q. Above the cutoff is positive?

7 A. We assume that.

8 Q. Below the cutoff is taken as negative.

9 A. Right. Then you have to do the clinical  
 10 trial.

11 Q. But is it generally the case that you  
 12 establish a cutoff, and that above the cutoff you  
 13 regard that as positive and below the cutoff you regard  
 14 it as negative?

15 A. That is immunoassay.

16 Q. Immunoassay. And is that the same for other  
 17 assays?

18 A. Give me example.

19 Q. Hybridization of nucleic acids.

20 A. That, I don't know. I'm not expert in that.

21 Q. Do you understand what the term  
 22 "Flaviviridae" means?

23 A. I know the term.

24 Q. What are Flaviviridae?

25

1 A. I would say like yellow fever.

2 Q. Does that include Flaviviruses?

3 MR. GRECO: Object to the form.

4 THE WITNESS: That, I don't know.

5 MR. RABINOWITZ: Q. Do you know whether  
 6 pestiviruses are part of the Flaviviridae?

7 MR. GRECO: Are you talking about  
 8 today, again, as of now?

9 MR. RABINOWITZ: Yes, as of now.

10 THE WITNESS: No, I think it's separate.

11 MR. RABINOWITZ: They're separate.

12 Q. Were they part of Flaviviridae at any time?

13 A. Earlier on, yes, I think so.

14 Q. Until when, as far as you know, what  
 15 pestiviruses --

16 A. I don't know, I don't remember.

17 Q. Were they separated out before 1995?

18 A. I don't recall.

19 Q. Do you recall whether that happened after  
 20 1990?

21 A. I don't recall.

22 Q. But do you recall that at one time  
 23 pestiviruses were considered part of Flaviviridae?

24 A. Very early on, yes.

25

1 MR. GRECO: Would this be a place for a  
 2 break?

3 MR. RABINOWITZ: Let's go off the record.

4 THE VIDEOGRAPHER: In the deposition of  
 5 Dr. George Kuo, this marks the end of Videotape 1.  
 6 Going off record. The time now is 11:06.

7 (Recess.)

8 THE VIDEOGRAPHER: In the deposition of  
 9 Dr. George Kuo, Ph.D., this marks the beginning of  
 10 Videotape 2. Going back on record. The time now is  
 11 11:16.

12 MR. RABINOWITZ: Q. Dr. Kuo, you told me  
 13 before we broke that you moved offices last year?

14 A. That's correct.

15 Q. Do you remember when in the year --

16 When you say last year, was that 1998?

17 A. That's correct.

18 Q. Do you remember when in 1998 you moved?

19 A. I remember it was more likely July.

20 Q. Do you think it might have been June, as  
 21 early as June?

22 A. People move different time, so we moved more  
 23 likely it's July.

24 Q. More likely July. Certainly not earlier

1 than June?

2 A. I don't remember.

3 As I recall, it is July.

4 Q. Okay, good. So you recall that you moved  
 5 offices yourself in July 1998.

6 Did the whole of Chiron move offices or only  
 7 part of it?

8 A. All the research people.

9 Q. All the research people together.

10 A. Yes.

11 Q. And do you know when the earliest move was  
 12 for part of that research group and when the latest  
 13 move was for the rest?

14 A. I don't know.

15 Q. Did any part of the research group move  
 16 before 1998?

17 A. I don't think so.

18 MR. RABINOWITZ: I would like to turn now to  
 19 the patents that issued to Chiron directed to HCV  
 20 nucleotides and tests using HCV nucleotides.

21 Actually, let me mark one of them now so we  
 22 know what we're talking about.

23 I'd like to ask the reporter to mark this as  
 24 Exhibit 200.

25

1 (WHEREUPON, DEPOSITION EXHIBIT 200 WAS  
 2 MARKED FOR IDENTIFICATION.)  
 3 MR. RABINOWITZ: Q. Dr. Kuo, I'm showing  
 4 you now what's been marked for identification as  
 5 Exhibit 200.  
 6 Do you recognize this document?  
 7 A. Yes.  
 8 Q. What is it?  
 9 A. It's like from the title.  
 10 Q. Is it Patent No. 5,714,596?  
 11 A. Yes.  
 12 Q. Are you an inventor of this patent?  
 13 A. Yes.  
 14 Q. I'd like to ask you about your involvement  
 15 in the prosecution of this patent before the Patent and  
 16 Trademark Office.  
 17 Did you have any role in preparing the  
 18 applications from which this patent issued?  
 19 A. It's more likely done by our patent  
 20 attorney.  
 21 Q. Did you play any part in preparing those  
 22 applications?  
 23 A. I don't recall.  
 24 Q. You don't recall whether or not you assisted  
 25

1 in preparing those applications?  
 2 A. That's correct.  
 3 Q. Do you recall whether you prepared any  
 4 writing for use by the patent attorney to draft the  
 5 application?  
 6 A. I don't recall.  
 7 Q. Did you provide any data to the patent  
 8 attorney for use in drafting the application?  
 9 A. Could you define for me the data, what  
 10 "data" means.  
 11 Q. Experimental results.  
 12 A. Experimental results. No, I don't think so.  
 13 I don't recall.  
 14 Q. Did you see the text of any of the  
 15 applications before they were filed with the Patent  
 16 Office?  
 17 A. Yes, I did, because I have to put my  
 18 signature.  
 19 Q. So did you see drafts of the applications  
 20 before they were submitted?  
 21 A. I think so.  
 22 Q. Were you asked to comment on the drafts?  
 23 A. Yes.  
 24 Q. Did you make any comments on the drafts?  
 25

1 A. I don't recall.  
 2 MR. GRECO: Is your question  
 3 specifically as to this patent, or are you talking  
 4 about any --  
 5 MR. RABINOWITZ: I'm talking about the  
 6 application that issued as this patent, Exhibit 200.  
 7 MR. GRECO: Okay, right. Just wanted  
 8 to clarify.  
 9 MR. RABINOWITZ: Q. So you recall that you  
 10 were provided with a copy of the -- of a version of the  
 11 application before it was filed in the Patent Office;  
 12 is that correct?  
 13 A. That's correct.  
 14 Q. And you read through the --  
 15 A. Yes.  
 16 Q. -- the application before it was filed in  
 17 the Patent Office?  
 18 A. That's correct.  
 19 Q. If you had seen anything that you disagreed  
 20 with, would you have mentioned that to anyone?  
 21 A. Yes, I will.  
 22 Q. Whom would you have mentioned it to?  
 23 A. More likely it will be our patent attorney.  
 24 Q. Do you recall whether you did make comments  
 25

1 to the patent attorney?  
 2 A. I don't --  
 3 MR. GRECO: You can answer that yes or  
 4 no, but don't reveal the substance of any discussions  
 5 with your attorneys.  
 6 Go ahead, you can answer.  
 7 THE WITNESS: No, I don't recall.  
 8 MR. RABINOWITZ: You don't recall.  
 9 Q. Did you agree with the statements in the  
 10 applications in the final form in which they were  
 11 submitted to the Patent Office?  
 12 A. Yes.  
 13 Q. Did you play --  
 14 Did you provide any assistance in responding  
 15 to comments by the patent examiners during the  
 16 examination of this patent?  
 17 A. I don't recall I did.  
 18 Q. Did you see copies of any of the papers sent  
 19 by the patent examiners?  
 20 A. I don't recall I saw that.  
 21 Q. You think you did not?  
 22 A. Yes, that's correct.  
 23 Q. Did you help prepare any of the responses  
 24 that were submitted to the Patent Office?  
 25

1 A. I don't recall I did.  
 2 Q. In other words, you think no?  
 3 A. No.  
 4 Q. As far as you can remember, no?  
 5 Did you provide any data for submitting to  
 6 the Patent Office during the course of prosecuting  
 7 these --  
 8 A. I don't recall.  
 9 Q. Does that mean as far as you remember, not?  
 10 A. That's correct.  
 11 Q. Let me direct your attention to the claims  
 12 of the '596 patent, Exhibit 200. In particular Claim 1  
 13 at Column 52.  
 14 MR. GRECO: 52.  
 15 MR. RABINOWITZ: You'll see that the column  
 16 numbers are provided at the top of each page.  
 17 Q. Are you an inventor of Claim 1?  
 18 MR. GRECO: Object to the form. Calls  
 19 for a legal conclusion.  
 20 You may answer.  
 21 THE WITNESS: Yes, I am.  
 22 MR. RABINOWITZ: Q. What about Claim 2, are  
 23 you an inventor of Claim 2?  
 24 MR. GRECO: Same objection.  
 25

1 You may answer.  
 2 THE WITNESS: Yes.  
 3 MR. RABINOWITZ: Q. Claim 3?  
 4 A. Yes.  
 5 Q. Claim 4?  
 6 A. Yes.  
 7 Q. Are you an inventor of Claim 5?  
 8 MR. GRECO: Same objection to all of  
 9 these questions.  
 10 You may answer.  
 11 THE WITNESS: Yes.  
 12 MR. RABINOWITZ: Q. Are you an inventor of  
 13 Claim 6?  
 14 A. Yes.  
 15 Q. Are you an inventor of Claim 7?  
 16 A. Yes.  
 17 Q. Are you an inventor of Claim 8?  
 18 A. Yes.  
 19 Q. Are you an inventor of Claim 9?  
 20 A. Yes.  
 21 Q. Are you an inventor of Claim 10?  
 22 A. Yes.  
 23 Q. Are you an inventor of Claim 11?  
 24 A. Yes.  
 25

1 Q. Are you an inventor of Claim 12?  
 2 A. Yes.  
 3 Q. Are you an inventor of Claim 13?  
 4 A. Yes.  
 5 Q. Are you an inventor of Claim 14?  
 6 A. Yes.  
 7 Q. Are you an inventor of Claim 15?  
 8 A. Yes.  
 9 Q. Are you an inventor of Claim 16?  
 10 A. Yes.  
 11 Q. Are you an inventor of Claim 17?  
 12 A. Yes.  
 13 Q. Are you an inventor of Claim 18?  
 14 A. Yes.  
 15 Q. Are you an inventor of Claim 19?  
 16 A. Yes.  
 17 Q. Are you an inventor of Claim 20?  
 18 A. Yes.  
 19 Q. Are you an inventor of Claim 21?  
 20 A. Yes.  
 21 Q. Are you an inventor of Claim 22?  
 22 A. Yes.  
 23 Q. Are you an inventor of Claim 23?  
 24 A. Yes.  
 25

1 Q. Are you an inventor of Claim 24?  
 2 A. Yes.  
 3 Q. Are you an inventor of Claim 25?  
 4 A. Yes.  
 5 Q. Are you an inventor of Claim 26?  
 6 A. Yes.  
 7 Q. Are you an inventor of Claim 27?  
 8 A. Yes.  
 9 Q. Are you an inventor of each and every one of  
 10 the claims of the '596 patent, Exhibit 200?  
 11 MR. GRECO: Objection.  
 12 THE WITNESS: Yes.  
 13 MR. RABINOWITZ: Fortunately, the other  
 14 patents have fewer claims.  
 15 Q. Let me direct your -- well, attention to the  
 16 '596 patent as a whole, and in particular to the  
 17 word -- the phrase "other viral agents" as it appears  
 18 in Claim 1. That's at Column 52, Line 11.  
 19 I beg your pardon, Line 10.  
 20 A. Okay.  
 21 Q. Does this patent define a special meaning  
 22 for the term "viral agents"?

23 MR. GRECO: Object to the form.  
 24 THE WITNESS: Could you read back the

1 question for me?

2 MR. RABINOWITZ: Certainly.

3 Q. Does the '596 patent, Exhibit 200, set forth  
4 a definition of the term "viral agent"?

5 A. It's just the virus cause the disease.

6 Q. Viral agent means a virus-causing disease?

7 A. Or a virus that cause disease.

8 Q. Refers generally to viruses causing disease?

9 A. No, that relate to hepatitis C.

10 Q. I'm sorry, are you saying that in the '596  
11 patent, the term "viral agent" means viruses causing  
12 disease?

13 A. Disease is hepatitis --

14 MR. GRECO: Let me get an objection in,  
15 please.

16 Object to the form of the question. Again,  
17 are you just asking him is there a definition in the  
18 spec, or are you asking him only about the claim?

19 I think the question's confusing when you  
20 say "in the patent."

21 MR. RABINOWITZ: I'm asking in the patent as  
22 a whole -- let's take the specification to start with.

23 Q. The specification is the portion that begins  
24 with Column 1 and ends at Column 52, Line 5.

25

1 Is there anywhere in the specification a  
2 definition of the term "viral agent"?

3 MR. GRECO: I object to the form.  
4 You're really asking his memory of the text of a very  
5 long patent. I don't think that's a very fair  
6 question.

7 You can answer it if you can remember.

8 THE WITNESS: Yeah, I could not -- I have  
9 to read back.

10 MR. RABINOWITZ: Take a look through the  
11 patent, if you wish. I'd like to know whether there is  
12 a definition of "viral agent" set forth in the patent.

13 THE WITNESS: In the Column 4, it's line  
14 about 20, the second paragraph.

15 MR. RABINOWITZ: Yes?

16 THE WITNESS: Yes, so they mention about  
17 the agent. Three different viruses in course of  
18 hepatitis.

19 MR. RABINOWITZ: Q. Is that a definition of  
20 the term "viral agent"?

21 MR. GRECO: Object to the form.

22 THE WITNESS: Well, again, don't ask me  
23 about a terminology here.

24 MR. RABINOWITZ: But I'm afraid I am asking  
25

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1 whether the patent sets forth a definition of "viral  
2 agent."

3 THE WITNESS: As I can understand, "viral  
4 agent" could be equal to the viruses that cause the  
5 hepatitis.

6 MR. RABINOWITZ: Q. So your testimony is  
7 "viral agent" means "viruses that cause hepatitis"?

8 A. No, that relate to the hepatitis C.

9 Q. What do you mean by related to hepatitis C?

10 MR. GRECO: Object to the form.

11 THE WITNESS: It have a homology to the  
12 hepatitis C sequence.

13 MR. RABINOWITZ: Q. Okay. Just continue.  
14 You've identified Column 4, Line 20. See if there's  
15 anywhere else in the specification that provides a  
16 definition of the term "viral agent."

17 MR. GRECO: You want him to read the  
18 entire patent? I mean, it's your time, but, I mean, it  
19 doesn't seem like a very productive use of it.

20 THE WITNESS: So as I can say, people  
21 interchange the "viral agent" with "viruses." So that  
22 depend on who is writing the patent and who is writing  
23 the article.

24 MR. RABINOWITZ: Q. So you're saying that  
25

1 in general, people interchange the term "viruses" and  
2 "viral agent"?

3 MR. GRECO: Object to the form.

4 THE WITNESS: From my point of view, yes.  
5 MR. RABINOWITZ: Q. And so my question is,  
6 does this patent say that the term "viral agent" is  
7 used more narrowly than that?

8 A. No, I didn't say that. I say the term --

9 The patent define very well we have  
10 hepatitis C patent. We present the sequence. Any

11 virus relate to this sequence is hepatitis C.

12 That is how we define.

13 Q. I understand that, but I'm directing your  
14 attention to Claim 1 now in Column 52, and it says --  
15 talks about hybridizing to the genome of hepatitis C  
16 virus or its complement relative to other viral agents.

17 And I'm trying to find out whether you can  
18 identify any part of the specification that defines a  
19 meaning for "other viral agents."

20 MR. GRECO: Object to the form.

21 Your question really is you're asking him to  
22 identify things in the specification. I don't see how  
23 he can do that without reading it. I mean, as many  
24 times as I've read that, I couldn't do that from  
25

1 memory.

2 That's literally what your question is  
 3 asking him, to look at the text of the patent and  
 4 identify everything that might be in there that relates  
 5 to that term.

6 MR. RABINOWITZ: Q. I'm asking if you're  
 7 aware that the specification provides any definition of  
 8 the term "other viral agents."

9 MR. GRECO: His recollection of the  
 10 specification? Because he obviously has not read it  
 11 sitting here today.

12 You could ask him if he recalls anything,  
 13 that's fair, but if you want to ask him literally  
 14 what's in there, he has to read it.

15 MR. RABINOWITZ: Q. As you sit here  
 16 today --

17 MR. GRECO: That's fine.

18 MR. RABINOWITZ: Q. -- are you aware of any  
 19 definition in the specification of the term "other  
 20 viral agent"?

21 A. I just answer the same, is that I will refer  
 22 to "viral agent" is equal to "viruses."

23 MR. RABINOWITZ: Okay. Thank you very much.  
 24 Q. Let me direct your attention to the term

25

1 "oligonucleotide" in Claim 1. That's on the first line  
 2 of Claim 1.

3 A. All right.

4 Q. Do you understand what the term  
 5 "oligonucleotide" means ordinarily in science?

6 A. Yes.

7 Q. What is an oligonucleotide as scientists  
 8 generally use that term?

9 A. It's a few nucleotide put together. It's  
 10 more than one nucleotide.

11 Q. Is there any limit on the size of an  
 12 oligonucleotide --

13 A. That depend on how you define it. So you  
 14 have to define. Is it 10 oligonucleotide, or 20  
 15 oligonucleotide?

16 Q. Do you understand the term "polynucleotide"  
 17 as that term is used ordinarily by scientists?

18 A. Yes.

19 Q. As scientists ordinarily use the terms, is  
 20 there any difference between the meaning of  
 21 "oligonucleotide" and "polynucleotide"?

22 A. That is another operational, practical  
 23 meaning.

24 Q. What is the operational difference between  
 25

1 "oligonucleotide" and "polynucleotide"?

2 A. Insulin is only 50 amino acid. Are you  
 3 going to say that is polypeptide or are you going to  
 4 say it's a protein?

5 Q. I'm afraid I must ask you to answer the  
 6 question.

7 A. So that depend on how you define. Some  
 8 people will say 50 is enough to call polynucleotide,  
 9 but some people will say no, that is still  
 10 oligonucleotide.

11 Q. Are you saying that in general,  
 12 polynucleotides are used for bigger nucleotide --  
 13 bigger sequences?

14 A. Yeah, in general, that is the truth.

15 Q. And oligonucleotides are used for smaller  
 16 sequences?

17 A. Yes.

18 Q. Is there a conventional cutoff between an  
 19 oligonucleotide and a polynucleotide, in size?

20 A. As I understand, there is no cutoff.

21 Q. You mean no fixed cutoff?

22 A. I don't think so.

23 Q. Would you accept that most scientists would  
 24 use -- or would you accept that scientists would use

1 oligonucleotide for a nucleotide sequence less than,  
 2 say, 150 nucleotides long?

3 A. That, I just answer you earlier on. So are  
 4 you going to say insulin is a protein or a polypeptide?

5 Q. I'm interested in what you would say,  
 6 Dr. Kuo.

7 A. So that is also define. I think it's how  
 8 you're going to define it.

9 So some people will say that is oligo, some  
 10 people will say, no, that's a polynucleotide.

11 Q. Do you agree that "oligonucleotide" and  
 12 "polynucleotide," as used in general, do not have  
 13 exactly the same meaning?

14 MR. GRECO: Object to the form.

15 THE WITNESS: I will say that is not a  
 16 general question. Exact the same? I don't say that is  
 17 a correct one. You ask me absolute answer, I cannot do  
 18 that.

19 MR. RABINOWITZ: Q. But you agree that --

20 A. Polynucleotide could be oligonucleotide.

21 But oligonucleotide, more likely people  
 22 won't call is a polynucleotide.

23 So it's a practical.

24 Q. And is the reason for that that

25

1 "oligonucleotides" is a term used to refer to smaller  
 2 nucleotide sequences?

3 A. In general.

4 Q. And "polynucleotides" is used to refer to  
 5 larger nucleotide sequences?

6 A. In general, but there's no absolute cutoff.

7 Q. Dr. Kuo, let me direct your attention to  
 8 Column 9, Line 47.

9 Would you read to yourself the first  
 10 sentence of that paragraph.

11 A. Yes.

12 Q. Do you agree that the term "polynucleotide"  
 13 as used in this patent refers to a nucleotide sequence  
 14 of any length?

15 MR. GRECO: Object to the form.

16 THE WITNESS: That is defined in here.

17 You can set up the definitions, as I just  
 18 mentioned. Oligonucleotide, some people will say  
 19 polynucleotide. Polynucleotide, some people will say  
 20 oligonucleotide.

21 But in here, you have to define it.

22 MR. RABINOWITZ: Q. And I'm asking you to  
 23 tell me how -- what's the meaning of the term  
 24 "oligonucleotide."

25

1 A. The meaning is just as printed in here.

2 Q. And do you agree the meaning is "a  
 3 nucleotide sequence of any length"?

4 A. Yes, we just print it.

5 Q. Thank you. Let me direct your attention to  
 6 Column 10, Lines 28, 29 and 30.

7 MR. GRECO: Look at the whole paragraph  
 8 if you want. He's going to ask you about 28, 29 and  
 9 30.

10 MR. RABINOWITZ: Yes, of course. Read any  
 11 other part of the patent that you wish to read to  
 12 enable you to understand the portion I'm going to  
 13 direct -- I'm directing your attention to.

14 MR. GRECO: He's referring to the  
 15 paragraph beginning -- I guess it's the one, "As used  
 16 herein"?

17 MR. RABINOWITZ: Yes, it begins "As used  
 18 herein."

19 THE WITNESS: Yes, I've finished.

20 MR. RABINOWITZ: Q. Do you agree that the  
 21 term "oligonucleotide" as used in the '596 patent  
 22 refers to "a nucleotide sequence of any length"?

23 A. When you say "any length," such as defined  
 24 in this paragraph. That is defined already here, so.

25

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1 Q. That's what I'm asking you about.

2 A. But I cannot say "any length." It's already  
 3 defined in this paragraph.

4 Q. And do you agree that the patent --

5 A. I agree with this paragraph.

6 MR. RABINOWITZ: I'm sorry, I'm going to ask  
 7 you to let me finish the question before you answer it,  
 8 and then maybe you want to wait a moment so that your  
 9 attorney can make an objection if he wants to, and then  
 10 we'll wait for you to finish your answer completely  
 11 before we move on to the next question.

12 Q. Do you agree that the term "oligonucleotide"  
 13 as used in this patent, refer to "a nucleotide sequence  
 14 of any length?"

15 A. My answer is it's already defined in this  
 16 paragraph. So that is the definition of  
 17 "oligonucleotide."

18 Q. Bearing in mind that definition, do you  
 19 agree or disagree that --

20 A. But within this paragraph --  
 21 (Simultaneous discussion.)

22 MR. GRECO: Wait till he finishes his  
 23 question.

24 MR. RABINOWITZ: Q. Bearing in mind the

1 definition set forth at Column 10 in the paragraph  
 2 beginning at Line 28, do you agree or disagree that "an  
 3 oligonucleotide" refers to "a nucleotide sequence of  
 4 any length"?

5 MR. GRECO: Object to the form.

6 THE WITNESS: I don't agree your "any  
 7 length" question, because already defined in here.

8 MR. RABINOWITZ: Q. And what do you  
 9 disagree about "any length"?

10 A. Because "any" could be you will define as  
 11 one or two. So this no mention about two here. So I  
 12 will say my answer still inside this paragraph.

13 Q. Are you saying that there's a minimum size  
 14 for an oligonucleotide?

15 A. I will say yes.

16 Q. What is the minimum size for an  
 17 oligonucleotide, as used in this patent?

18 A. This is defined in here.

19 Q. Well, please, tell me.

20 A. And then later on.

21 Q. So you've told me that your understanding of  
 22 the term "oligonucleotide" as used in this patent,  
 23 conveys that there is a minimum length in order to  
 24 qualify as an oligonucleotide.

25

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1 MR. GRECO: Object to the form.  
 2 MR. RABINOWITZ: Q. Is that correct?  
 3 A. I will say yes. Yes.  
 4 Q. How large must a nucleotide sequence be to  
 5 count as an oligonucleotide as that term is used in  
 6 this patent?  
 7 MR. GRECO: Object to the form.  
 8 THE WITNESS: I think we define in the  
 9 claim here, so I cannot memorize everything.  
 10 MR. RABINOWITZ: Q. Based on Column 10, the  
 11 paragraph beginning at Line 28, how large must a  
 12 oligonucleotide be -- a nucleotide sequence be to  
 13 qualify as an oligonucleotide?  
 14 MR. GRECO: Same objection.  
 15 THE WITNESS: We set up the upper limit  
 16 here. So that is still my answer.  
 17 You try to ask me about minimum. So that is  
 18 not in this paragraph, so I cannot answer your  
 19 question.  
 20 MR. RABINOWITZ: Q. I'm just asking you  
 21 whether there is or is not a minimum limit.  
 22 A. But in this paragraph, we didn't say there's  
 23 a minimum.  
 24 Q. Okay. So do you consider that there is a  
 25

1 minimum in order to qualify as an oligonucleotide?  
 2 A. That is -- outside this paragraph?  
 3 Q. As the term "oligonucleotide" is used in  
 4 this patent.  
 5 MR. GRECO: Object to the form.  
 6 THE WITNESS: Well, the definition of  
 7 "oligonucleotide" is "more than one." So I will say  
 8 more than one, people can call that as oligonucleotide.  
 9 MR. RABINOWITZ: Q. So anything from --  
 10 anything that is two nucleotides or longer can be an  
 11 oligonucleotide. Is that right?  
 12 A. That is from my understanding. But your  
 13 definition could be different from mine, or from -- or  
 14 different from Richard's.  
 15 Q. I'm asking about the definition in the  
 16 patent, the way it's used in the patent.  
 17 MR. GRECO: I'm not sure what the  
 18 question is now.  
 19 MR. RABINOWITZ: Q. As the term  
 20 "oligonucleotide" is used in Exhibit 200, do you agree  
 21 that the lower limit is two nucleotides?  
 22 A. I will say that is correct.  
 23 Q. Is there an upper limit?  
 24 A. And that is defined in here.  
 25

1 Q. And what is -- what does that tell you?  
 2 MR. GRECO: Objection.  
 3 MR. RABINOWITZ: Q. Is there an upper limit  
 4 or not?  
 5 A. Yeah, I don't think there is an upper limit.  
 6 Q. You think there is no upper limit?  
 7 A. No.  
 8 MR. RABINOWITZ: Counsel, just for  
 9 information, I'm interested in the basis of your  
 10 objection as to form.  
 11 MR. GRECO: You're asking him what  
 12 terms mean in the patent, which is, as you know, a  
 13 legal issue that's determined by the court based on  
 14 things other than the witness's personal knowledge or  
 15 personal understanding. And so when you use the term  
 16 "how the term is used in the patent," that really  
 17 implies that you're asking for a construction of it.  
 18 Plus it's also you're asking him what  
 19 literally it says. I mean, which I think is, you know,  
 20 not really a proper question for a witness.  
 21 MR. RABINOWITZ: Thank you.  
 22 Q. Let me refer you back to Claim 1, Column 52.  
 23 Do you have an understanding what the term "purified  
 24 preparation of an oligonucleotide" means?  
 25

1 MR. GRECO: Same objection.  
 2 THE WITNESS: Yes, it is a --  
 3 "Purify" means it's different from the  
 4 starting material.  
 5 MR. RABINOWITZ: Q. Okay. Are there any  
 6 particular criteria that have to be satisfied to make  
 7 an oligonucleotide preparation purified?  
 8 A. No, different people can have different  
 9 standard.  
 10 Q. So if I have a preparation of an  
 11 oligonucleotide and I'm trying to determine whether it  
 12 falls within the scope of this claim or not, do you  
 13 agree that it must be purified, at least in the meaning  
 14 of this patent, before it can qualify -- before it can  
 15 fall within the scope of Claim 1?  
 16 A. You have to --  
 17 MR. GRECO: Objection. Go ahead.  
 18 THE WITNESS: Sorry. You have to read  
 19 the whole sentence. You cannot take half the sentence  
 20 and try to ask me question.  
 21 MR. RABINOWITZ: Q. Read the whole sentence  
 22 then.  
 23 A. Yes. So your oligonucleotide got to purify  
 24 is not like original, and then the oligonucleotide is  
 25

1 capable of selectively hybridizing to the genome of the  
 2 hepatitis C virus.

3 So that is a whole sentence.

4 Q. Have you completed your answer?

5 A. Yes.

6 Q. So if I have an oligonucleotide preparation  
 7 that does satisfy all the other requirements of the  
 8 claim, do you agree that it must be purified in order  
 9 to fall within the scope of this claim?

10 MR. GRECO: Object to the form.

11 THE WITNESS: So then you have to define  
 12 "purify" for me, then I can answer.

13 MR. RABINOWITZ: Q. Do you have an  
 14 understanding of what "purified" means in this claim?

15 A. Yes.

16 Q. What does "purified" mean --

17 A. It means away from the starting material.

18 Q. Dr. Kuo, let me just restate the question  
 19 because I think you began answering before I'd quite  
 20 finished.

21 What does "purified" mean in this claim?

22 MR. GRECO: Same objection.

23 THE WITNESS: It's different from the  
 24 starting material.

25

1 MR. RABINOWITZ: Q. And does that mean that  
 2 any difference between the oligonucleotide and the  
 3 starting material will suffice to make it purified?

4 A. So we're talking about oligonucleotide here.  
 5 Okay? Oligonucleotide, if you synthesize it chemically  
 6 from four different bases, so that is the starting  
 7 material. And when you synthesize it, then if you do  
 8 anything to be different from the starting material,  
 9 that is purification.

10 Q. Okay. Is it possible to make a purified  
 11 preparation of an oligonucleotide from naturally  
 12 occurring sources?

13 A. Yes, I will guess so. This is from the  
 14 nature source, yes.

15 Q. And what must you do to make it -- to  
 16 qualify as purified if you're doing it from natural  
 17 sources?

18 A. Define the nature source for it.

19 Q. How about naturally occurring hepatitis C  
 20 virus?

21 A. Then you separate, you have to separate the  
 22 protein from the nucleic acid, and that is a  
 23 purification.

24 Q. So if it is separated from the proteins,

25

1 then it's purified?

2 A. I didn't say -- proteins is one of the  
 3 example. You give me an example, I tell you.

4 Q. Okay. My example is --

5 A. If virus, then I say it is separate from the  
 6 nucleic acid from the protein.

7 Q. My example is, the oligonucleotide is  
 8 separated from the proteins of the hepatitis C virus.  
 9 Is that purified?

10 MR. GRECO: Object to the form.

11 You may answer.

12 THE WITNESS: You give me the hepatitis  
 13 virus. I say that is one of the purification.

14 MR. RABINOWITZ: Q. So that would be  
 15 purified?

16 A. I would say yes, in my own definition.

17 Q. Let me direct your attention to the term  
 18 "selectively hybridizing" in Claim 1 of the '596  
 19 patent.

20 A. Yes.

21 Q. Do you understand what that term means?

22 A. Yes.

23 Q. What does "selectively hybridizing" mean in  
 24 Claim 1 of the '596 patent?

25

1 MR. GRECO: Objection. You may answer.  
 2 THE WITNESS: Will hybridize to the  
 3 hepatitis C genome.

4 MR. RABINOWITZ: Q. Have you completed your  
 5 answer?

6 A. Yes. Or it complementary related, just the  
 7 whole sentence.

8 Q. I'm sorry, just would you tell me again what  
 9 "selectively hybridizing" means?

10 A. To genome of hepatitis C virus or its  
 11 complement relative to other viral agent.

12 Q. And what does that mean?

13 A. That means it's either hybridized through  
 14 hepatitis C genome or its cDNA, for example, that is  
 15 complementary or as a viral agent.

16 Q. So are you saying that any oligonucleotide  
 17 that hybridizes to HCV or its complements will  
 18 selectively hybridize within the meaning of this claim?

19 MR. GRECO: Same objection. Go ahead.

20 THE WITNESS: Yes, I think so, yes.

21 MR. RABINOWITZ: Q. In order for an  
 22 oligonucleotide to qualify as selectively hybridizing  
 23 to the genome of a hepatitis C virus or its complement,  
 24 must the sequence of that oligonucleotide be the same

1 as hepatitis C virus or its complement?

2 A. That is not -- you don't have to be 100% complement.

3 Q. Right.

4 A. You say "same." You have to define for me what "same" means.

5 Q. Is there a minimum percentage identity that it must satisfy?

6 A. No. We didn't say that.

7 Q. So how does a scientist tell whether an oligonucleotide is capable of selectively hybridizing to a hepatitis C virus or complement?

8 A. Yes, your oligonucleotide will hybridize to hepatitis C or its complement.

9 Q. And is that sufficient to show that it selectively hybridizes --

10 A. Yes, under certain condition, the hybridization will occur.

11 Q. What does "relative to other viral agents" mean with respect to selective hybridization in this claim?

12 MR. GRECO: Same objection.

13 THE WITNESS: That means any other viruses will still hybridize.

25

1 MR. RABINOWITZ: Q. You say the oligonucleotide will hybridize to other viruses as well?

2 A. I didn't say that. I say when the oligo will hybridize, the nucleotide will hybridize to the hepatitis C or the complementary or as a virus agent.

3 Q. So are you saying it is necessary to do a comparison between hybridizing to HCV and hybridizing to other viral agents?

4 MR. GRECO: Object to the form.

5 THE WITNESS: No, I didn't say that.

6 MR. RABINOWITZ: Well, then, I'm afraid I don't understand your answer.

7 Q. I'm asking you whether there is a test one can do to determine whether an oligonucleotide is capable of selectively hybridizing to the genome of an HCV or its complement relative to other viral agents.

8 Do you know of such a test?

9 A. If the test -- what kind of test? Give me example of other tests.

10 Q. I'm asking you whether you know of a test one can do.

11 A. No, there's so many tests, so how can I answer?

25

1 Q. Well, name one.

2 A. Blood sample, for example. Sample from the blood bank.

3 Q. How would you go about testing whether an oligonucleotide satisfies this?

4 A. Yes, you can extract the nucleic acid and do the hybridization and then see if there's -- if any genome or nucleic acid will hybridize to this oligonucleotide.

5 Q. And if it does, does that show that the oligonucleotide is capable of selectively hybridizing to HCV or its complement relative to other viral agents?

6 A. Yes, if there is HCV there, I think the oligonucleotide will hybridize it, and that is a selectively hybridize.

7 MR. RABINOWITZ: I'd like to go off the record.

8 THE VIDEOGRAPHER: Going off record. Time now is 12:02.

9 (Discussion held off the record.)

10 (Luncheon recess: 12:02 p.m.)

25

1 AFTERNOON SESSION  
(1:03 p.m.)

2 THE VIDEOGRAPHER: Going back on record.

3 Time now is 1:03.

4 MR. RABINOWITZ: Q. Dr. Kuo, let me direct your attention back to Exhibit 200, the '596 patent, Column 19, Line 44 to 53.

5 And I'm still asking with respect to the meaning of "capable of selectively hybridizing to the genome of a hepatitis C virus or its complement relative to other viral agents."

6 Will you read that section to yourself?

7 MR. GRECO: Could you state the lines again, please? Column 19?

8 MR. RABINOWITZ: Yes, Column 19, Lines 44 to 53.

9 THE WITNESS: To this spot?

10 MR. RABINOWITZ: Q. Have you had an opportunity to read that paragraph?

11 A. Yes, I did.

12 Q. Now, turning back to Claim 1 in Column 52, does that clarify the meaning for you of "capable of selectively hybridizing to the genome of a hepatitis C virus or its complement relative to other viral

25

1 agents"?

2 MR. GRECO: Object to the form.

3 THE WITNESS: So what is your question  
4 again?5 MR. RABINOWITZ: Q. Does the paragraph in  
6 Column 19 that you've just read explain the meaning of  
7 "capable of selectively hybridizing to the genome of a  
8 hepatitis C virus or its complement relative to other  
9 viral agents"?

10 MR. GRECO: Object to the form.

11 THE WITNESS: Explain partially.

12 MR. RABINOWITZ: Q. What does it explain  
13 about that meaning?14 A. That under this condition, can the probe  
15 selectively hybridize to hepatitis C.16 So this is another operational. If it  
17 doesn't, then you have to change. So the most  
18 important thing in here is the hepatitis C virus  
19 genome.

20 MR. RABINOWITZ: I see.

21 THE WITNESS: So if you want to detect  
22 the virus, if under certain condition it doesn't  
23 selectively hybridize, then you have to find a way.  
24 But still it still bond to it, I will say yes.

25

1 MR. RABINOWITZ: Q. So how do you tell when  
2 you've achieved conditions which -- under which  
3 selective binding takes place?

4 A. That is you have to do the clinical trial.

5 Q. You have to do a clinical trial?

6 A. Yes.

7 Q. And until you've done a clinical trial, it's  
8 not --

9 A. No, you confirm by other, by other means.

10 This region, you have a question, then you can always  
11 use the other region to do it.12 Q. So, again, you identified two ways now I  
13 think in which you say one can determine whether you  
14 have conditions which permit selective hybridization.15 Firstly, you say you can do a clinical  
16 trial. Is that right?17 A. Oh, if you want, yeah. If you can -- you  
18 want to do it -- how good your assay is, you can run a  
19 lot of different sample.20 Q. And short of a clinical trial, how else  
21 could you determine whether you have found conditions  
22 under which the hybridization is selective to HCV  
23 relative to other viral agents?

24 A. You can use --

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1 Genome is very long, about 10kb, so you can  
2 have a lot of different region to confirm that if this  
3 region doesn't selectively hybridize, or you have  
4 question about selectivity, then you can always use  
5 other region to do it.6 Q. And so you say, we must do it by trial and  
7 error?8 A. Not necessarily trial and error. You have  
9 the sequence in your hand, so it's not trial and error  
10 here.11 Q. So how does one determine which part of the  
12 HCV genome sequence you selectively hybridize?13 A. You can look at the sequence and then make a  
14 judgment.

15 Q. And how do you make that judgment?

16 A. Well, as I mentioned earlier on, I'm not an  
17 expert in the nucleic acid, so what I answer to you is  
18 from my opinion. So there's a lot of different way to  
19 do it.20 Q. And in your opinion, what is one way of  
21 doing it?22 A. Yeah, you just use other region to confirm.  
23 If you find something bind to one region, do you see  
24 another one to bind another region?

25

1 So, give you example, like hepatitis B  
2 surface antigen test. Why is it called sandwich assay?  
3 You ask the same question two times.4 One monoclonal antibody are bind to the  
5 surface antigen. You ask another antibody, does this  
6 antibody bind to the surface antigen.

7 So that is in general practice.

8 Q. Let me direct your attention to Column 28,  
9 Lines 4 through 19.

10 A. Yes.

11 Q. Again, with respect to Claim 1, does this  
12 section that you just read explain the meaning of  
13 "capable of selectively hybridizing to the genome of a  
14 hepatitis C virus or its complement relative to other  
15 viral agents"?16 MR. GRECO: Objection.  
17 You may answer.18 THE WITNESS: As I just mentioned, I'm no  
19 expert in the PCR or other things. This is just very  
20 simple description of one of the way to detect the  
21 hybridization.22 MR. RABINOWITZ: Q. So that shows a way of  
23 detecting hybridization?24 A. One of the way. There are several ways to  
25

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1 do it, so this describes one way to do it.  
 2 Q. Does this way described in Column 28,  
 3 Lines 4 to 19, help you to determine whether the  
 4 binding is selective or non-selective?  
 5 MR. GRECO: Object to the form.  
 6 THE WITNESS: Well, your so-called  
 7 selective, you have to confirm it one way or the other.  
 8 So without confirming it, so I -- I just  
 9 cannot answer your question.  
 10 MR. RABINOWITZ: Q. So --  
 11 A. They say, yes, use this condition, we are  
 12 selectively hybridizing. That is my answer.  
 13 Q. So do I understand correctly that you say  
 14 that if you find binding, you will need to do further  
 15 experiments to determine whether -- to confirm whether  
 16 it is selective or not?  
 17 A. If necessary. But you cannot say there is  
 18 no binding.  
 19 MR. RABINOWITZ: I'd like to ask the  
 20 reporter to mark a document. I think we are up to 201  
 21 now.  
 22 (WHEREUPON, DEPOSITION EXHIBIT 201 WAS  
 23 MARKED FOR IDENTIFICATION.)  
 24 MR. RABINOWITZ: Q. Dr. Kuo, I'd like to  
 25

1 And please read that and anything else in  
 2 the declaration that you need to read to understand it  
 3 and then let me know when you've had an opportunity to  
 4 do that.  
 5 A. Okay.  
 6 Q. Have you had a chance to read the paragraph  
 7 and the rest of the declaration?  
 8 A. Yes.  
 9 Q. Now, turning to Paragraph 5, Dr. Brammar  
 10 says:  
 11 Under (sic) "conditions of gradually  
 12 increasing stringency, you would expect  
 13 readily to find conditions under which  
 14 the oligonucleotide remains hybridized  
 15 only to the HCV RNA. If such a  
 16 condition does not prevail, then the  
 17 oligonucleotide does not selectively  
 18 hybridise to the HCV genome."  
 19 Do you see that passage in Paragraph 5?  
 20 A. Yes, I do.  
 21 Q. Do you agree with that statement?  
 22 MR. GRECO: Object to the form.  
 23 Go ahead.  
 24 THE WITNESS: Partially.  
 25

1 direct your attention to the document that has been  
 2 marked Exhibit 201.  
 3 Have you ever seen this document before?  
 4 A. The whole document?  
 5 Q. The whole document or any part of it.  
 6 A. I don't recall I see this.  
 7 Q. Can I ask you to turn to the second page  
 8 from the top, the one that's marked with Page No. 1 on  
 9 the bottom.  
 10 Can you read the title that's underlined and  
 11 in bold about one-third of the way down the page?  
 12 MR. GRECO: Why don't you just read it.  
 13 MR. RABINOWITZ: Q. Do you agree that this  
 14 is entitled "Declaration of William J. Brammar under 37  
 15 C.F.R. Section 1.132"?  
 16 A. Yes. I see it right now.  
 17 Q. And do you see that there's a date written  
 18 in hand towards the top, 7/9/96?  
 19 A. That's correct.  
 20 Q. I'd like to direct your attention to Page 3,  
 21 Paragraph 5 of the declaration.  
 22 A. Which paragraph?  
 23 Q. Paragraph 5. Would you read that to  
 24 yourself, please.  
 25

1 Q. And what do you disagree with?  
 2 A. If you are dealing with virus agent or some  
 3 infectious agent which cause human disease and then you  
 4 want to develop the assay for it, for example,  
 5 hepatitis C, you want to develop the screening method  
 6 for hepatitis C, this maybe is not the proper way to do  
 7 it.  
 8 Q. What are the limitations of this method of  
 9 doing it?  
 10 A. Well, because this is based on just one  
 11 hybridization. So if this fail, virus, as I mention,  
 12 is 10kb, you can always use other region to do it.  
 13 Q. So in your opinion this is not a reliable  
 14 way of determining this?  
 15 A. I didn't say that. I said depend on what  
 16 you want to do.  
 17 Q. Do you agree that if you do not find  
 18 conditions under which the oligonucleotide remains  
 19 hybridized only to the HCV RNA, then the  
 20 oligonucleotide does not selectively hybridize to the  
 21 HCV genome?  
 22 A. That is also is operational definition.  
 23 Doesn't hybridize is different meaning. So different  
 24 depend on how you -- what kind of condition.  
 25

1 that has been placed in front of you.  
 2 Have you ever seen this document before or  
 3 any part of it?  
 4 A. I don't recall.  
 5 Q. Do you see that on Page 1, the document has  
 6 been labeled "Amendment"?  
 7 A. Yes.  
 8 Q. And that a date has been written in by hand,  
 9 February 27, 1995?  
 10 A. Yes.  
 11 Q. And do you see that in the -- about  
 12 one-third down the first page, there's written  
 13 "Serial No. 08/040,564"?

14 A. Yes.  
 15 Q. Would you turn to the last page. Do you see  
 16 that under the signature there's written the name  
 17 Kenneth M. Goldman?  
 18 A. Yes.  
 19 Q. Do you know who Kenneth M. Goldman is?  
 20 A. Used to be a patent lawyer at Chiron.  
 21 Q. I see. I'd like to direct your attention to  
 22 Page 11. There are three points marked in bold with  
 23 bullets next to them. The second bullet point, would  
 24 you read that to yourself, please.  
 25

1 If you have the right condition, then it  
 2 will hybridize it. If you have no right condition, it  
 3 won't hybridize.  
 4 Q. So do you mean that unless you specify the  
 5 conditions, this isn't meaningful?  
 6 MR. GRECO: Object to the form.  
 7 THE WITNESS: Well, this is just sort of  
 8 very general description. Gradually increasing  
 9 stringency condition. What that means? Didn't mention  
 10 anything.  
 11 So you can find a way to see the  
 12 hybridization, you can find a way you don't see the  
 13 hybridization. So doesn't mean it's not selectively  
 14 hybridizing, so that is my answer to this.  
 15 MR. RABINOWITZ: Q. So in your view what  
 16 should have been specified here to remedy --  
 17 A. I don't know. I'm not an expert witness to  
 18 write this, so I really don't know. I have no opinion.  
 19 MR. RABINOWITZ: I'd like to ask the  
 20 reporter to mark this next document as document 202.  
 21 (WHEREUPON, DEPOSITION EXHIBIT 202 WAS  
 22 MARKED FOR IDENTIFICATION.)  
 23 MR. RABINOWITZ: Q. Dr. Kuo, I'd like to  
 24 direct your attention to a document marked Exhibit 202  
 25

1 THE WITNESS: Yes.  
 2 MR. GRECO: Object also as taking out  
 3 of context of what that is. I don't think it's  
 4 something you can agree or disagree with.  
 5 THE WITNESS: I agree with this  
 6 statement.

7 MR. RABINOWITZ: Q. Do you agree that for  
 8 an oligonucleotide to selectively hybridize to a genome  
 9 of an HCV or its complement relative to other viral  
 10 agents, that it must contain a sequence that is  
 11 identical or complementary to the HCV genome?

12 THE WITNESS: Could you read back the  
 13 question?

14 (Record read.)

15 THE WITNESS: I don't agree, what you are  
 16 just saying. You don't need 100% complementary.

17 MR. RABINOWITZ: Q. What percentage  
 18 complementarity do you need?

19 A. That depend how long oligonucleotide you are  
 20 using.

21 Q. Do you agree that for an oligonucleotide to  
 22 be capable of selectively and detectably hybridizing to  
 23 the genome of a hepatitis C virus or its complement  
 24 relative to other viral agents, that the

25

1 oligonucleotide must contain the sequence that is  
 2 unique when compared to other viral agents?  
 3 MR. GRECO: Object to the form.  
 4 THE WITNESS: That is -- "unique" also is  
 5 relative term. So it's not absolute terminology.  
 6 "Unique" means it's relative compared with  
 7 other.

8 MR. RABINOWITZ: Q. Well, do you agree that  
 9 the oligonucleotide must contain a sequence which is  
 10 unique when compared to other viral agents?  
 11 A. Not necessarily. I just mention could be  
 12 it's very similar, or there's partially complementary  
 13 to it.

14 As I just mentioned, hybridization is based  
 15 on hydrogen binding and hydrogen binding is not  
 16 absolute. Same as when you have antibody bind to the  
 17 epitope. There's no such thing as absolute. You can  
 18 have change in affinity, but antibody still bind to it.

19 Q. Have you completed your answer?

20 A. Yes.

21 Q. So you disagree --

22 A. I disagree.

23 Q. -- with that statement?

24 A. No, your statement.

25

1 MR. RABINOWITZ: Let me have marked  
 2 Exhibit 203 for identification.  
 3 Excuse me, can I just take a look at that.  
 4 I just want to be sure that this isn't a marked-up  
 5 copy.

6 (WHEREUPON, DEPOSITION EXHIBIT 203 WAS  
 7 MARKED FOR IDENTIFICATION.)

8 MR. RABINOWITZ: Q. Dr. Kuo, have you seen  
 9 this document before?

10 A. Yes, I did.

11 Q. What is this document?

12 A. It's the patent application for the  
 13 recombinant non A, non B virus polynucleotide.

14 Q. Now, going back to Exhibit 202, Page 11, the  
 15 second bullet point refers, in the third line, to  
 16 Page 13, Lines 3 to 19 of the '714 application.

17 Do you see that on Exhibit 203 there's a  
 18 number been stamped on the first page on the top?

19 I'm directing you now to Exhibit 203, the  
 20 top page. The first page of 203. Do you see the  
 21 number 122714?

22 A. Yes.

23 Q. Will you understand if I refer to this as  
 24 the '714 application, that I'm referring to

25

1 Exhibit 203?

2 A. Okay.

3 Q. If you could turn to Page 13 and read to  
 4 yourself Lines 3 to 19.

5 MR. GRECO: Well, I think that's a  
 6 paragraph that begins on the bottom of Page 12, so I  
 7 think --

8 MR. RABINOWITZ: And anything else in that  
 9 application --

10 MR. GRECO: I think he should at least  
 11 read the full paragraph.

12 THE WITNESS: Yes.

13 MR. RABINOWITZ: Q. Does the paragraph  
 14 you've just read in Exhibit 203 teach an  
 15 oligonucleotide that is capable of selectively  
 16 hybridizing to the genome of a hepatitis C virus or its  
 17 complement relative to other viral agents?

18 MR. GRECO: Objection.

19 THE WITNESS: Just give you the example.  
 20 Stable way to do it, but not the only way to do it.

21 MR. RABINOWITZ: Q. Does it teach the idea  
 22 of an oligonucleotide that is capable of selectively  
 23 hybridizing to an HCV or its complement relative to  
 24 other viral agents?

1 A. Again, I think it says you are define  
 2 selectively and detectably hybridize. So you have to  
 3 define your criteria for me in order for me to answer.  
 4 Q. Well, I'm asking you whether you can find in  
 5 this paragraph teachings that convey to you the idea of  
 6 selectively hybridizing to HCV relative to other viral  
 7 agents?

8 A. It's a certain way, yes, you can do it.

9 Q. Will you point out to me the parts of this  
 10 paragraph that teach that?

11 MR. GRECO: Object to the form.

12 THE WITNESS: I just mention there's a  
 13 lot of just known technology in here. For example, you  
 14 can use a Tom Maniatis --

15 (Reporter interruption.)

16 THE WITNESS: You can use the textbook  
 17 edited by Tom Maniatis.

18 MR. GRECO: "Tom Maniatis" I think he's  
 19 saying.

20 MR. RABINOWITZ: That's M-A-N-I-A-T-I-S.

21 Q. Is that the reference to Page 13, Line 20?

22 A. No, it says 1982.

23 Q. Are you referring to Line 20 on Page 13  
 24 there?

25

1 A. Line 20.  
 2 Q. Okay. Apart from Line 20, is there any  
 3 other part of that paragraph that conveys the idea of  
 4 an oligonucleotide capable of selectively hybridizing  
 5 to HCV or its complement relative to other viral  
 6 agents?

7 A. As I just mentioned earlier, I'm not a  
 8 nucleic acid expert here, so when I read this, I would  
 9 say, yes, partially will tell you how to do it.  
 10 But I'm not doing it, so I cannot answer --  
 11 really answer your question.

12 Q. So I'm asking you to identify for me the --  
 13 or read to me the sections that convey that idea.

14 A. As I just say, I'm not an expert. If you  
 15 are asking me about protein chemistry or immunoassay, I  
 16 can tell you, but here is -- all are in nucleic acid  
 17 testing. So really I'm not in a position to answer  
 18 your question.

19 Q. Well, are you saying that you're unable to  
 20 identify --

21 A. Not unable, but I think if you --

22 MR. RABINOWITZ: I'm sorry, let me finish my  
 23 question.

24 Q. Are you saying that you are unable to

25

1 identify particular sentences in that paragraph which  
 2 teach the idea of an oligonucleotide that is capable of  
 3 selectively hybridizing to HCV relative to other viral  
 4 agents?

5 MR. GRECO: Objection to the form.

6 THE WITNESS: Well, whole paragraph  
 7 already describe a lot of different thing. It's in  
 8 this paragraph.

9 And why you ask me, say, okay, you identify.  
 10 It's already described here. This whole paragraph.

11 You compare with the Genebank, doing some of  
 12 the -- compared to the run sequence of other virus  
 13 agents. Then you can do different thing. Determine  
 14 complementary by known in art and discussed in Tom  
 15 Maniatis.

16 So mismatch of duplex can treat with S1  
 17 nuclease. So that is already tell you a lot.

18 MR. RABINOWITZ: Q. The reason I'm focusing  
 19 on this paragraph is that in Exhibit 202, the Chiron  
 20 patent attorney argued that this paragraph taught the  
 21 idea of an oligonucleotide that was capable of  
 22 selectively and detectably hybridizing to the genome of  
 23 a hepatitis C virus or its complement relative to other  
 24 viral agents.

25

1 And the Chiron patent attorney focused on a  
 2 teaching that the nucleic acid contains a sequence that  
 3 is identical or complementary to the HCV genome.

4 Now, do you see on Page 13 at Line 3, the  
 5 sentence that reads:

6 "In addition, the sequence of the  
 7 region from which the polynucleotide is  
 8 derived is identical to or  
 9 complementary to a sequence which is  
 10 unique to the NANBV genome"?

11 MR. GRECO: Objection to the form of that  
 12 question, among other things. I also object to the  
 13 characterization of the patent attorney's amendment and  
 14 what he was saying there. But I'm not sure you have a  
 15 question at the end of that long recitation.

16 MR. RABINOWITZ: Will you read back the  
 17 question at the end of that long recitation.

18 (Record read.)

19 MR. RABINOWITZ: Q. Do you see that  
 20 sentence, Dr. Kuo? The sentence beginning on Page 13  
 21 of Exhibit 203, Line 3, "In addition." One word in to  
 22 Line 3.

23 A. So what is your question?

24 Q. So taking that sentence together with the  
 25

1 sentence -- the two sentences beginning on Line 11,  
 2 "The sequence can also be compared to the known  
 3 sequences of other viral agents, including those which  
 4 are known to cause hepatitis," and he gives some  
 5 examples. "The correspondence or non-correspondence of  
 6 the derived sequence to other sequences can also be  
 7 determined by hybridization under the appropriate  
 8 stringency conditions."

9 Taking that portion of this paragraph, does  
 10 that, taken together, convey the idea of an  
 11 oligonucleotide that is capable of selectively  
 12 hybridizing to HCV or its complement relative to other  
 13 viral agents?

14 MR. GRECO: Objection.

15 THE WITNESS: Yes, I still believe it is  
 16 capable of selectively and detectably hybridizing to a  
 17 genome of the hepatitis C virus.

18 MR. RABINOWITZ: Q. And that's conveyed by  
 19 paragraph -- this paragraph on Page 13 of Exhibit 203?  
 20 Right?

21 A. This is one way to prove it.

22 Q. And is one way to prove it, hybridizing it  
 23 under appropriate stringency conditions?

24 A. Yes. That is, yes.

25

1 Q. And are you looking for an oligonucleotide  
 2 that under stringent conditions will hybridize to HCV  
 3 and will not hybridize to other viruses?  
 4 MR. GRECO: Object to the form.  
 5 THE WITNESS: Again, we are not talking  
 6 about absolute here. I think we are talking about  
 7 relative hybridization here.

8 Under this condition that your  
 9 oligonucleotide hybridize to hepatitis C, same time we  
 10 hybridize hepatitis A or hepatitis B. Very simple  
 11 question. So if the answer is no, then you find other  
 12 way to do it, but doesn't mean it's not selectively  
 13 hybridized to hepatitis C.

14 MR. RABINOWITZ: Q. But if it selectively  
 15 hybridizes to hepatitis C, then it ought to hybridize  
 16 to hepatitis C and not to hepatitis A. Is that right?

17 A. There is no such thing as absolute in  
 18 biological system here, sir.

19 Q. And is that why you disagreed with  
 20 Professor Brammar's statement in Exhibit 201?

21 A. I didn't disagree. That is one way to do  
 22 it.

23 But what we are doing is biomedical research  
 24 here. We are not dealing with theoretical biochemistry

25

145

146

1 here.

2 Q. Let me read again from Exhibit 201,  
 3 Paragraph 5.

4 MR. GRECO: 201.

5 MR. RABINOWITZ: Exhibit 201, Paragraph 5.  
 6 Under (sic) "conditions of gradually  
 7 increasing stringency, you would expect  
 8 readily to find conditions under which  
 9 the oligonucleotide remains hybridized  
 10 only to the HCV RNA."

11 That's on Page 3, Paragraph 5.

12 Do you have it there?

13 A. Yes.

14 Q. Under (sic) "conditions of gradually  
 15 increasing stringency, you would expect  
 16 readily to find conditions under which  
 17 the oligonucleotide remains hybridized  
 18 only to the HCV RNA. If such a  
 19 condition does not prevail, then the  
 20 oligonucleotide does not selectively  
 21 hybridise to the HCV genome."

22 MR. GRECO: I think you have to keep  
 23 reading. To be fair, you have to read the whole  
 24 context there.

25

1 MR. RABINOWITZ: As a negative control,  
 2 one would use an oligonucleotide of the  
 3 same length in base-composition, but  
 4 with a randomized or scrambled  
 5 sequence, and perform a parallel  
 6 hybridization to a similar panel of  
 7 nucleic acids."

8 Q. Is it wrong to say that you would expect  
 9 readily to find conditions under which the  
 10 oligonucleotide remains hybridized only to the HCV RNA?

11 A. As I say, Dr. Brammar just keep his opinion  
 12 about ideal situation here. So he doesn't consider in  
 13 the blood bank setting or in the laboratory setting.

14 This is theoretical approach.

15 He is partially right, he is partially  
 16 wrong, as I can see it.

17 Q. And let me just ask you the same thing about  
 18 the continuation.

19 "If such a condition does not  
 20 prevail, then the oligonucleotide does  
 21 not selectively hybridise to the HCV  
 22 genome."

23 Do you consider that to be partially right  
 24 and partially wrong as well?

25

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1 A. That is my answer.

2 MR. RABINOWITZ: Thank you, sir.

3 Q. I'd like to take you back to Exhibit 200,  
4 the '596 patent, and I'm going to ask you to explain to  
5 me what the term "hepatitis C virus" means in this  
6 patent.

7 A. In general?

8 Q. In this patent, and I'm going to direct your  
9 attention to Columns 6 through 8 of Exhibit 200, the  
10 '596 patent.

11 MR. GRECO: Wait. Now I'm not sure  
12 what your question is anymore.

13 MR. RABINOWITZ: I'll restate the question.

14 Q. Let me direct your attention to those  
15 columns of the patent first.

16 MR. GRECO: All right. You want him to  
17 look at Columns 6 through 9.

18 THE WITNESS: So what is your question?

19 MR. RABINOWITZ: Q. My first question is  
20 whether you've had an opportunity to read Columns 6  
21 through 8.

22 A. That too long for me to read. I think maybe  
23 better you ask a question one by one.

24 MR. GRECO: If you ask your question

25

1 first, then he can speed up the reading.

2 MR. RABINOWITZ: Maybe we'll be able to  
3 focus it a little bit.

4 Q. Firstly, when you and your co-inventors  
5 filed the applications that issued as this patent, did  
6 you consider that hepatitis C virus included  
7 hepatitis A virus?

8 A. No.

9 Q. Did you consider that hepatitis C virus  
10 included hepatitis B virus?

11 A. No.

12 Q. Did you consider that hepatitis C virus  
13 included hepatitis D virus?

14 A. No.

15 Q. Did you consider that hepatitis C virus  
16 included hepatitis G virus?

17 A. There is no such thing as hepatitis G. It  
18 just is a virus looking for the disease, as you know.  
19 It doesn't cause the hepatitis.

20 Q. Is there such a virus that is sometimes  
21 called hepatitis G virus?

22 A. Eventually, if someone abandons that, I  
23 think.

24 Q. But is there a virus that some scientists  
25

1 refer to as hepatitis G virus?

2 A. I guess.

3 Q. Did you consider that virus to be included  
4 within your understanding of hepatitis C virus?

5 A. We defined hepatitis C virus with this  
6 definition.

7 Q. I'm just asking about your understanding.

8 Did you understand that hepatitis C virus included what  
9 is sometimes called hepatitis G virus?

10 A. As you know, the reason people call non A,  
11 non B hepatitis is because this is hepatitis, and when  
12 you test with hepatitis A and hepatitis B, there's no  
13 marker. So any hepatitis is not caused by A, not  
14 caused by B, it's called non A, non B hepatitis.

15 And later on people find hepatitis delta and  
16 hepatitis E. And that is not our patent here. We  
17 define hepatitis C in certain way. So we already put a  
18 frame there. So this is the frame we claim, this is  
19 hepatitis C.

20 Q. So is it accurate that you did not consider  
21 hepatitis C to include what is now called hepatitis E?

22 A. No. We don't think so.

23 Q. And did you consider that hepatitis C  
24 includes what is now called hepatitis G?

25

1 A. As I say, G is not cause hepatitis.

2 Q. So it doesn't include that virus?

3 A. I would say no.

4 Q. Are you familiar with a virus called BVDV?

5 A. Yes.

6 Q. Did you consider that hepatitis C virus  
7 includes BVDV?

8 A. We only consider human disease here.

9 Q. So does that mean you did not consider  
10 hepatitis C virus to include BVDV?

11 A. That is caused the bovine disease.

12 Q. Is it correct that you did not consider  
13 hepatitis C virus to include BVDV?

14 A. Well, I think that is in general we consider  
15 that. We only deal with human disease here.

16 Q. Is that a "Yes," you did not consider it to  
17 include BVDV?

18 A. That, I think so, yes.

19 Q. I have a finite list of viruses, so we'll  
20 get through to the end of them. I just want to  
21 confirm, is it true that you did not consider  
22 hepatitis C virus to include West Nile virus?

23 A. Well, are we sit here to test my virology  
24 knowledge, or we are defending the patent? I think,

25

1 sir -- sir, I think, sir, we are wasting time here.  
 2 Q. I'll go through this as quickly as I can. I  
 3 have a few more questions of this kind and then we'll  
 4 go back to the patent.

5 A. Because if you ask my virology knowledge, I  
 6 learned it 20, 30 years ago. I really cannot answer  
 7 you. I think that is --

8 Q. Dr. Kuo, if you don't know the answer to a  
 9 question --

10 A. No, but it is unfair for you to ask me in  
 11 here to -- why me I cannot answer it. That is not --  
 12 I'm not coming here to take a medical board,  
 13 for example. Is that fair?

14 MR. GRECO: I think maybe you just need  
 15 to clarify. When you're asking "does it include," I  
 16 think the confusion may be are you asking is it  
 17 related, or is it something of that nature?

18 MR. RABINOWITZ: Let me clarify the question  
 19 in case there's any misunderstanding.

20 Q. I'm trying to identify what you and your  
 21 co-inventors considered in your minds that what you are  
 22 now calling hepatitis C virus would include and would  
 23 not include. And to help define the boundaries of  
 24 that, I'm trying to ask whether it -- whether your

25

1 idea, as you conceived hepatitis C virus, included  
 2 particular other viruses.

3 And that's why I'm asking whether hepatitis  
 4 C virus, as you envisioned it, would or would not  
 5 include certain other viruses.

6 This is certainly not a test of anyone's  
 7 virological knowledge, and I'm quite sure you've  
 8 forgotten much more virology than I will ever know.  
 9 But it's helpful to us for the purposes of this  
 10 litigation to clarify what you and your co-inventors in  
 11 your own minds considered that hepatitis C virus either  
 12 did include or did not include.

13 A. That's fair.

14 Q. And it's with that focus that I'm asking  
 15 these questions. And I know it's a little tedious and  
 16 I'm going to go through this as quickly as I can, and I  
 17 promise you there's a finite number which will help us  
 18 identify what you and your co-inventors considered to  
 19 yourselves that your hepatitis C virus covered, and  
 20 then once we've done that, we'll move on.

21 So let me just ask again, as you and your  
 22 co-inventors conceptualized hepatitis C virus, did you  
 23 consider that it included West Nile virus?

24 A. We only deal with the virus, or viruses. At  
 25

1 that time, we didn't know how many viruses called  
 2 non A, non B hepatitis. It caused human disease,  
 3 infect the human liver, and that is what we define.

4 So it is the hepatitis virus, and then we  
 5 call that is C. So we defined for the kind of genome  
 6 we are dealing with, so that is our territory here.

7 Q. Is it correct that West Nile virus was  
 8 identified at the time that you discovered hepatitis C  
 9 virus?

10 A. I don't know.

11 Q. I see. Were you aware of yellow fever virus  
 12 at the time that you discovered hepatitis C virus?

13 A. Yes.

14 Q. Did you and your co-inventors consider that  
 15 hepatitis C virus should include yellow fever virus?

16 A. My question for you, does yellow fever cause  
 17 hepatitis?

18 Q. Is that your answer?

19 A. Yes. Because you have to tell me, does that  
 20 cause hepatitis or not.

21 Q. Let me ask the question again. I'm trying  
 22 to identify whether when you were -- whether the way  
 23 that you envisioned hepatitis C virus, you intended to  
 24 include yellow fever virus within that name of

25

1 hepatitis C virus.

2 A. From my recollection, yellow fever virus  
 3 doesn't cause hepatitis, so we didn't -- I don't think  
 4 we would intend to include that.

5 Same as Epstein-Barr virus cause hepatitis,  
 6 but that is DNA virus.

7 Q. So the Epstein-Barr virus is not within  
 8 hepatitis C virus?

9 A. No.

10 Q. Nor is HIV?

11 A. No.

12 Q. Nor is herpes simplex virus?

13 A. We rule that out. That is when people  
 14 working on non A, non B hepatitis, herpes sometimes  
 15 cause hepatitis. So that is we know of.

16 In the field, people already automatic rule  
 17 this out.

18 Q. So in your mind, hepatitis C virus did not  
 19 include herpes simplex?

20 A. I don't think so.

21 Q. Nor human papilloma virus?

22 A. I don't think so.

23 Q. Nor -- I'm not sure whether we covered it,  
 24 nor yellow fever virus?

25

1 I'm sorry?

2 MR. GRECO: Did you ask him that  
3 already?

4 MR. RABINOWITZ: I'm not sure whether we got  
5 a clear answer for the record, so let me restate the  
6 question.

7 Q. Just to clarify, you did not consider that  
8 hepatitis C virus as you are naming it included yellow  
9 fever virus?

10 A. That is my opinion. What I answer here is  
11 my opinion. One of the inventor. You have to ask the  
12 other three. Other two, not three.

13 Q. But in your opinion, it did not include  
14 yellow fever virus?

15 A. Right.

16 MR. RABINOWITZ: Thank you. Is this an  
17 appropriate time for a break?

18 MR. GRECO: Uh-huh.

19 THE VIDEOGRAPHER: In the deposition of  
20 Dr. George Kuo, this marks the end of Videotape 2.  
21 Going off record, the time now is 2:03.

22 (Recess.)

23 THE VIDEOGRAPHER: In the deposition of  
24 Dr. George Kuo, this marks the beginning of

25

1 Videotape 3. Going back on record, the time now is

2 2:14.

3 MR. RABINOWITZ: Q. Dr. Kuo, let me draw  
4 your attention once again to Exhibit 200, which is the  
5 '596 patent, and I'm going to be asking you for the  
6 next little while about the meaning of hepatitis C  
7 virus.

8 Can I ask, the way hepatitis C virus is  
9 defined in this patent, is it confined to hepatitis C  
10 virus HCV-1?

11 A. No.

12 Q. It includes other strains of hepatitis C  
13 virus?

14 A. You mean a strain, what that means?

15 Q. Other isolates of hepatitis C virus.

16 A. I think so.

17 Q. So it's broader than HCV-1?

18 A. Because this is RNA virus, so RNA virus tend  
19 to mutate. So we say this is the virus related to this  
20 type of first isolate and cause the same disease. That  
21 is our definition.

22 Q. So HCV-1 was the first isolate, but your  
23 definition of HCV-1 includes other isolates as well?

24 A. That's correct.

25

1 Q. Does HCV-1 include only isolates isolated by  
2 1990, which was when the application was filed, or does  
3 it include isolates discovered afterwards as well?

4 MR. GRECO: Object to the form.

5 You said HCV-1 or HCV?

6 MR. RABINOWITZ: HCV.

7 MR. GRECO: Just HCV. I thought you  
8 said "1" in your question there.

9 MR. RABINOWITZ: I better repeat the  
10 question just in case I did.

11 Q. Does the definition of HCV in the patent  
12 include only isolates of HCV that were discovered up to  
13 1990, or does it include isolates of HCV that were  
14 discovered afterwards as well?

15 MR. GRECO: Object to the form.

16 THE WITNESS: Personally, I will say we  
17 are including the future isolate. Without our  
18 sequence, nobody can isolate the other.

19 MR. RABINOWITZ: Q. So your definition  
20 includes isolates found after 1990, does it?

21 A. Yes. And the people accept that, use the  
22 same terminology, too.

23 Q. Let me direct you to Column 6, Line 62. Do  
24 you see there where it says:

25

1 "The term HCV also includes new  
2 isolates of the same viral species"?

3 A. Right.

4 Q. What is a viral species?

5 A. That is a virus species that relate to  
6 hepatitis C.

7 Q. Are there criteria for determining whether  
8 one virus and another virus are members of the same  
9 species?

10 A. Then you have to define a species for me,  
11 because that is --

12 What we try to say is we have a prototype or  
13 a type 1 sequence, and we believe this is the cause of  
14 hepatitis C. And so if someone isolate another  
15 isolate, also cause the hepatitis C and it has got the  
16 same gene organization, then we will say that is the  
17 hepatitis C.

18 Q. Does the term "hepatitis C virus" in your  
19 patent only include viruses that cause hepatitis?

20 A. From my thinking, yes.

21 Q. So if I'm trying to classify a virus to see  
22 whether it falls within hepatitis C virus or not, do I  
23 have to establish that it causes hepatitis before I can  
24 classify it as an HCV?

25

1 A. Well, that is --  
 2 You are doing experiment. You try to do it,  
 3 so that is your decision, not my decision.  
 4 Q. I'm asking -- I'm trying to establish what  
 5 tests a virus must pass to be considered an HCV within  
 6 the meaning of the patent. I'm asking, is one  
 7 requirement that it must cause hepatitis?

8 MR. GRECO: Object to the form.

9 You may answer. Go ahead.

10 THE WITNESS: In here we also describe  
 11 the defective virus particle, and are you going to tell  
 12 me the defective virus particle of hepatitis C is not  
 13 hepatitis C?

14 MR. RABINOWITZ: I'm actually going to ask  
 15 you.

16 Q. Is a defective particle of hepatitis C --

17 A. I will say yes, because they have the same  
 18 genome organization, so some reason it's defective.

19 Q. Do defective interfering particles cause  
 20 hepatitis?

21 A. From definition, it's no.

22 Q. So does it follow that the definition of  
 23 hepatitis C virus includes viruses that do not cause  
 24 hepatitis?

25

1 A. The "defective particle" is operational  
 2 terminology here. When you say is it defective, for  
 3 you? Not necessarily defective if you inject that to  
 4 me. So "defective" is a different meaning, and we  
 5 think that defective virus particle is a nucleic acid;  
 6 that could be infectious.

7 So it's the definition is an operational  
 8 definition.

9 Q. So I'm not quite clear that I understand  
 10 your response to the question whether in order to pass,  
 11 to qualify as a hepatitis C virus, as the term is used  
 12 in the patent, whether a virus must cause hepatitis or  
 13 whether it need not cause hepatitis.

14 MR. GRECO: Object to the form.

15 You may answer.

16 THE WITNESS: That, I -- if you ask my  
 17 opinion, I just described to you. The defective  
 18 particle you find in your body is still is the virus.

19 You know, when you isolate the purified  
 20 virus polio, only 10% are infectious, 90% defective in  
 21 general. So are you going to say that defective is not  
 22 a polio virus? Still, it's the polio virus.

23 So certain way you can define. Okay, if you  
 24 isolate nucleic acid from defective particle, do they

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1 have the same -- very similar sequence to the  
 2 hepatitis C? If the answer is yes, then it's  
 3 hepatitis C. If they have the same genome  
 4 organization, then obviously, yes, it's hepatitis C.

5 MR. RABINOWITZ: Okay.

6 Q. Let me direct your attention to Column 6,  
 7 the very last sentence beginning on Line 66.

8 Do you see that it says, "The terms non A,  
 9 non B hepatitis and hepatitis C may be used  
 10 interchangeably herein"?

11 A. Right.

12 Q. Does the "term non A, non B hepatitis"  
 13 include hepatitis D?

14 A. No.

15 MR. GRECO: Objection.

16 Go ahead, you can answer.

17 MR. RABINOWITZ: Q. Is hepatitis D not a  
 18 non A, non B hepatitis?

19 A. It's already named hepatitis D.

20 Q. Is that included within non A, non B  
 21 hepatitis?

22 A. No, hepatitis D discovered after B.

23 The reason called non A, non B is you  
 24 don't -- there's no marker for A, no marker for B, so

1 there's a blank there. And then later on people find  
 2 hepatitis D, and hepatitis E. So --  
 3 Q. So what is the meaning of the term "non A,  
 4 non B hepatitis"?

5 A. Well, that is just in general. In the early  
 6 Seventies and middle of Seventies, when you have a test  
 7 of hepatitis A and B.

8 Q. What does "non A, non B" mean then?

9 A. It's not A, not B.

10 Q. Does that include hepatitis D?

11 MR. GRECO: Objection. As to when?

12 THE WITNESS: That time, maybe. But as  
 13 you know, hepatitis D --

14 How much do you know about hepatitis delta?

15 MR. RABINOWITZ: We're not going to explore  
 16 my knowledge at this deposition. I'm just going to ask  
 17 you some questions.

18 THE WITNESS: Because hepatitis delta is  
 19 hepatitis D surface antigen.

20 So when you assay with the hepatitis B test,  
 21 it will fall into the B. So not a B, not A is called  
 22 non A, non B.

23 MR. RABINOWITZ: Q. Does non A, non B  
 24 include hepatitis E?

25

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1 MR. GRECO: Say that again, please?  
 2 MR. RABINOWITZ: Q. Does non A, non B  
 3 hepatitis include hepatitis E?  
 4 A. We define it here very narrow. It's the  
 5 blood-borne hepatitis. It's not A and not B. And we  
 6 call, when we isolated the genome, then we named  
 7 hepatitis C. So that is all.

8 Q. But I'm asking you about the term "non A,  
 9 non B hepatitis." Does that include hepatitis E?

10 MR. GRECO: Objection.

11 THE WITNESS: That is -- as I said, we  
 12 didn't use that term. That has been used by the  
 13 hepatologist.

14 MR. RABINOWITZ: Q. You do understand the  
 15 meaning of the term "non A, non B hepatitis"?

16 A. Yes.

17 Q. And are you able to tell me whether it  
 18 includes hepatitis E or not?

19 A. Right now, it's not.

20 Q. At any stage, did non A, non B hepatitis  
 21 include hepatitis E?

22 A. When people isolate hepatitis E, they find  
 23 out that is not -- they didn't call hepatitis C. They  
 24 call hepatitis E.

25

1 Q. But was that virus included in the general  
 2 term "non A, non B hepatitis" at any time?  
 3 A. I don't think people use -- include that.  
 4 Q. Are you familiar with a virus called GBVB?  
 5 A. Yes. Not "familiar." I know this term.  
 6 Q. Would that be included within the term  
 7 "non A, non B hepatitis"?

8 A. Does that cause virus -- cause disease?

9 Q. I'm asking for, in your opinion, is GBVB  
 10 included in the term "non A, non B hepatitis"?

11 MR. GRECO: Objection to the form.

12 THE WITNESS: If the sequence is very  
 13 similar, there's a homology; and if we can pick up with  
 14 the assays basically for hepatitis C, then we will say  
 15 that is part of C.

16 MR. RABINOWITZ: Q. And do you know whether  
 17 it is part of C?

18 A. No, it doesn't pick up by our immunoassay,  
 19 so I don't think that is included.

20 Q. And are you saying that hepatitis C is the  
 21 same as non A, non B hepatitis?

22 A. Blood-borne.

23 Q. Blood-borne.

24 A. Yes.

25

1 Q. Are there forms of non A, non B hepatitis  
 2 that are not blood-borne?

3 A. People believe so.

4 Q. What viruses cause --

5 A. The so-called community-acquired non A,  
 6 non B hepatitis.

7 Q. And what viruses cause community-acquired  
 8 non A, non B hepatitis?

9 A. Right now it's caused by the same virus. So  
 10 although it's called "community-acquired," actually  
 11 it's transmit by the blood product.

12 Q. So are you aware of any viruses that cause  
 13 non A, non B hepatitis except for hepatitis C?

14 A. That is different from hepatitis C, then  
 15 they should use other nomenclature.

16 Q. So as far as the scientific literature is  
 17 concerned --

18 A. Yeah, they will say non A to G, or non A to  
 19 F, or something.

20 Q. Does the scientific community identify  
 21 viruses other than hepatitis C as non A, non B  
 22 hepatitis viruses?

23 MR. GRECO: Objection.

24 THE WITNESS: No, they call non A to E or

1 non A to G, or something. That's why you have a  
 2 hepatitis G. Hepatitis F has been named by the virus  
 3 in mid-1990.

4 MR. RABINOWITZ: Q. Is hepatitis F a non A,  
 5 non B hepatitis viruses?

6 A. It's not part of our non A, non B here. We  
 7 don't define that. We define our non-hepatitis C very  
 8 clear. Positive strain RNA virus cause hepatitis.

9 Q. I understand you've defined what hepatitis C  
 10 is, but I'm asking whether the term "non A, non B  
 11 hepatitis" includes hepatitis F?

12 A. Again, I just want to answer your question  
 13 clearly. The reason they call non A, non B is if you  
 14 don't have a hepatitis A marker, you don't have a  
 15 hepatitis B marker, and the hepatologists just threw in  
 16 the garbage can and call it non A, non B hepatitis.  
 17 So it's not our terminology.

18 Q. Does hepatitis F have a hepatitis A marker?  
 19 A. Hepatitis? It disappear. Once someone

20 claim, but no longer exists.

21 Q. So hepatitis F is not hepatitis A. Right?

22 A. I don't think so.

23 Q. Hepatitis F is not hepatitis B?

24 A. I don't think so.

1 Q. So doesn't it follow that hepatitis F is  
 2 part of that, what you've described as the garbage can  
 3 non A, non B hepatitis?

4 A. That --

5 MR. GRECO: Objection.

6 Go ahead. You can answer.

7 THE WITNESS: It's a mixture.

8 But when we work on this project, we don't  
 9 know how many viruses we are dealing with. We clone  
 10 one of the virus. Then later on we find out this virus  
 11 cause 90 or 95% of the so-called non A, non B  
 12 hepatitis.

13 MR. RABINOWITZ: Q. Do you know what causes  
 14 the other 5 to 10%?

15 A. Other virus.

16 Q. What are the other --

17 A. Maybe. We don't know.

18 Q. But some viruses?

19 A. Maybe, or unknown reason.

20 Q. Let me direct your attention to Column 7,  
 21 the first sentence, which says:

22 "HCV is a viral species of which  
 23 pathogenic strains cause blood-borne  
 24 non A, non B hepatitis."

25

1 Are there non-pathogenic strains of  
 2 hepatitis C virus?

3 A. So you consider defective particle is not  
 4 pathogenic, or no?

5 Q. Would you say that the defective particle is  
 6 non-pathogenic?  
 7 A. I would say neither. I will not answer, say  
 8 absolutely it is not pathogenic, but I will not say it  
 9 is pathogenic.

10 As I mentioned, if you isolate nucleic acid,  
 11 that could be infectious.

12 Q. What is an attenuated strain?

13 A. That is like when you take a polio, as an  
 14 example. Sabin polio strain is attenuated.

15 Q. What does "attenuated" mean?

16 A. Well, "attenuated" is English. I give you  
 17 example like polio. Sabin virus is attenuated virus.

18 Q. And what enables it to be classified as  
 19 attenuated, what properties mark a virus as attenuated?

20 A. If you take a polio example, that means it  
 21 doesn't cause disease.

22 Q. Okay. So an attenuated strain is a strain  
 23 that doesn't cause disease?

24 A. But that -- hold onto that. One of the few  
 25

1 hundred thousand in some people still cause disease.  
 2 So are you going to say that is not pathogenic?

3 Q. I'm interested in your opinions.

4 A. No. This is science, there is no absolute.  
 5 So I just want to tell you, don't force me to give you  
 6 zero. There's no such thing.

7 Sabin is very safe vaccine, been used  
 8 on million, million people. But some people do pick up  
 9 the disease. In Daly City, just south of San  
 10 Francisco, there's one case.

11 Q. So you say that --

12 Are you able to say whether an attenuated  
 13 strain of HCV would be pathogenic, or are you saying  
 14 that you can't say one way or the other?

15 A. I cannot say one way or the other.

16 Q. Okay. Let me direct your attention to  
 17 Column 7, the sentence beginning on Line 8,  
 18 "Therefore."

19 A. "Therefore." Yes.

20 Q. Do you see it says:

21 "...there are multiple  
 22 strains/isolates, which may be virulent  
 23 or avirulent, within the HCV species."

24 What does that mean?

25

1 A. Again, someone write a patent, so if you ask  
 2 my opinion, I think that is -- I can explain to you,  
 3 but not necessarily it's the correct answer.

4 Q. Well, please explain.

5 A. Take hepatitis C as the case. People  
 6 infected with the C will recover, maybe 20%. 80% will  
 7 become chronic. Among those chronic patients, some are  
 8 healthy carrier. The liver function is normal. But if  
 9 you detect the nucleic acid as a marker, you do detect  
 10 that. But some patient will have abnormal liver  
 11 function, ALT will jump up and down.

12 So my interpretation will be the one they  
 13 call virulent form is cause the disease. But that is  
 14 not absolute. Virulent strain of this infect to other  
 15 people, may become avirulent.

16 Q. Does "avirulent" mean it doesn't cause  
 17 disease?

18 A. Not necessarily doesn't cause disease, cause  
 19 mild disease.

20 So, again, like Sabin virus as example. The  
 21 virus duplicate. Still in your immune system. So you  
 22 cannot say virus didn't replicate in the vaccinee. It  
 23 does.

24 Q. Okay. Let me draw your attention to the

25

1 sentence beginning at the end of the third line of  
 2 Paragraph 7 -- of Column 7.

3 "As shown infra, the HCV genome is  
 4 comprised of RNA."

5 A. Which line?

6 Q. Line 3 to 4, Column 7.

7 A. So we're back again. Okay.

8 Yes.

9 Q. Is it -- in order to classify a virus as an  
 10 HCV virus, must it have an RNA genome?

11 A. So you are talking about the virus exists in  
 12 the nature, or nucleic acid generate in a test tube?

13 Q. I'm talking about the virus.

14 A. Yes, I will assume that is true.

15 Q. What I'm trying to discover is, are there a  
 16 number of tests or a number of criteria that the virus  
 17 must satisfy so that we can classify it as an HCV  
 18 within the meaning of the patent.

19 And so I'm going to be going through here  
 20 trying to identify what a virus must be or must look  
 21 like, or must possess in order to qualify as an HCV.

22 A. I understand that. And also my -- I try to  
 23 explain a lot of different thing even outside this  
 24 patent to you so I make myself clear.

25

1 Q. Well, clarity is very good. So we'll do it  
 2 in as much detail as it needs to be clear.

3 But, sir, you agree that to classify -- to  
 4 classify a virus as hepatitis C within the meaning of  
 5 the patent, it must be an RNA virus?

6 A. Yes.

7 Q. You agree it need not cause disease?

8 A. That is a question mark, as I just explain  
 9 to you. It doesn't cause disease in you, not  
 10 necessarily in other people.

11 Q. But you wouldn't look for proof that it  
 12 causes disease in order to label it as an HCV?

13 MR. GRECO: Objection to the form.

14 MR. RABINOWITZ: Q. Is that right?

15 A. But as I just mentioned, are you going to do  
 16 the experimental transmit to other people to prove it  
 17 causes the disease, or just take one; look, we have RNA  
 18 virus here, and he is healthy, there's no disease, and  
 19 so it's not hepatitis C?

20 I say no, I don't accept that.

21 Q. So you're saying evidence of disease would  
 22 not be necessary?

23 A. That's correct.

24 Q. Let me direct you to -- well, let me ask

25

173

174

1 you, as HCV is defined in this patent, is it necessary  
 2 for a virus to be a positive-stranded RNA virus to  
 3 qualify as an HCV?

4 A. We also cover complementary.

5 Q. I'm talking about the virus now. Would one  
 6 have to show that it is a positive-stranded RNA virus  
 7 to satisfy the definition that's set forth here?

8 MR. GRECO: Object to the form.

9 THE WITNESS: I think so. But also we  
 10 have to define very clear the sequence gene  
 11 organization.

12 MR. RABINOWITZ: Q. We'll get to that in a  
 13 while. I'm just trying to find out whether positive  
 14 strandedness is a criterion for being a hepatitis C  
 15 virus.

16 You say it is a criterion?

17 A. Right.

18 Q. Let me draw your attention to Column 8,  
 19 Lines 14 to 15. It says:

20 "In addition, it is believed that  
 21 the genome would be a positive-stranded  
 22 RNA."

23 A. Yes.

24 Q. Some of the statements in the patent are

1 prefaced by words like "it is believed" or "it is  
 2 expected."

3 Does this mean -- "it is believed," does  
 4 this mean that it is a necessary property of the HCV  
 5 genome?

6 MR. GRECO: Objection to the form.

7 THE WITNESS: You better ask our  
 8 attorney. This is a legal terminology, so I cannot  
 9 answer your question.

10 MR. RABINOWITZ: Q. When you read it  
 11 yourself, do you understand whether it's necessary or  
 12 not necessary for an HCV to have a positive-stranded  
 13 RNA genome?

14 MR. GRECO: Objection.

15 THE WITNESS: It's one of the criteria,  
 16 not the only criteria.

17 MR. RABINOWITZ: Q. So you're saying it  
 18 must have a positive-stranded RNA genome?

19 A. But a positive strand doesn't have a coding  
 20 sequence, doesn't have a nucleatized sequence, a  
 21 homology to hepatitis C. So I don't think that is the  
 22 criteria. So it's one of the criteria.

23 Q. So it's one of the criteria?

24 A. Yes.

25

175

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1 Q. I'm now going to ask you about amino acid  
2 homology to the HCV-1 amino acid sequence.

3 I'm going to direct your attention to  
4 Column 8, the first paragraph, beginning on Line 1 and  
5 ending on Line -- I believe it's 15.

6 Please let me know when you've had a chance  
7 to read that paragraph.

8 A. Yes.

9 Q. Let me read you the first three sentences.  
10 It says:

11 "Different strains, isolates or  
12 subtypes of HCV are expected to contain  
13 variations at the amino acid and  
14 nucleic acids compared with HCV1. Many  
15 isolates are expected to show much  
(i.e., more than about 40%) homology in  
16 the total amino acid sequence compared  
with HCV1. However, it may also be  
17 found that there are other less  
18 homologous HCV isolates."

19 Is there a threshold amino acid homology  
20 with HCV-1 that is required to be classified as an HCV?

21 MR. GRECO: Objection to the form.

22 THE WITNESS: No, I don't think so. This

1 is just arbitrary number.

2 MR. RABINOWITZ: Q. And is it your view  
3 that a virus can be an HCV even if it's less homologous  
4 than 40% at the amino acid level?

5 A. That depend on which part of the polypeptide  
6 you want to compare. You are going to compare the  
7 conserve region, or compare with the envelope region?

8 So if you compare with the envelope region,  
9 you may be able to find more than 40% difference.

10 Q. Well, the sentence, "However, it may also be  
11 found that there are other less homologous HCV  
12 isolates" --

13 A. Right.

14 Q. -- does that indicate that a virus can  
15 qualify as an HCV even if it's less homologous than  
16 40%?

17 A. You're playing a number here. I think we  
18 have to look at the function of this virus.

19 If this virus got the same property, cause  
20 the disease and have a certain region, is a conserve,  
21 for example, a nucleocapsid region, and there's some  
22 protease region, because those are important for the  
23 virus, they are conserved. The other particle could be  
24 mutant, could be different, but cause the same disease

25

1 and get the same genome organization, I will say that  
2 is hepatitis C.

3 Q. Okay. Now, going back to that second  
4 sentence in Paragraph 8, it says:

5 "Many isolates are expected to show  
6 much (i.e., more than about 40%)  
7 homology in the total amino acid  
8 sequence compared with HCV1."

9 Do you agree that's talking about overall  
10 homology in the total amino acid sequence of the one  
11 virus compared with -- of the candidate virus compared  
12 with HCV-1?

13 A. Yes, I agree, from the region here, yes.

14 Q. And then it says:

15 "However, it may also be found that  
16 there are other less homologous HCV  
17 isolates."

18 Does that indicate that a candidate virus  
19 might classify as an HCV on other criteria, even if  
20 it's less than 40% homologous in the total amino acid  
21 sequence to HCV-1?

22 A. But you have to read further. You cannot  
23 take from the context and ask me the question.

24 Could you just read further up, and then you

1 answer to yourself.

2 Q. That's why I say "might" qualify based on  
3 other criteria. I'm just trying to find out --

4 I'm going to take one criterion after the  
5 other and ask whether it's essential. Now, you've  
6 testified that it's essential that it be an RNA virus;  
7 it's essential that it be a positive-stranded virus or  
8 an A virus; it's not essential that it cause disease.

9 Right?

10 A. In certain condition.

11 Q. Now I'm trying to find out whether it's  
12 essential that it must be at least 40% homologous at  
13 the amino acid level.

14 And based on what is said here, I'm asking  
15 whether you agree, it need not necessarily be 40% or  
16 more homologous in the total amino acid sequence to  
17 HCV-1.

18 MR. GRECO: Objection to the form.

19 THE WITNESS: I could not answer your  
20 question, because it is confusing for me here, so I  
21 don't know.

22 MR. RABINOWITZ: Okay.

23 Q. Then it says:

24 "These would be defined as HCV

25

1 according to various criteria..."  
 2 Now, do you agree that the word "these" is  
 3 referring to "other less homologous HCV isolates?"  
 4 A. Don't ask me the English -- the attorney's  
 5 English here. I just don't understand your question,  
 6 so I'm sorry.

7 Q. Okay. Well, can you tell me what you  
 8 understand by the rest of the paragraph beginning  
 9 "These would be defined" and ending at the end of the  
 10 paragraph?

11 MR. GRECO: Objection to the form.  
 12 THE WITNESS: It says, open reading frame  
 13 of approximately 9,000 nucleotide to approximately  
 14 12,000 nucleotide, encoding a polyprotein similar in  
 15 size to that of hepatitis HCV-1.

16 So then you define an encoded polyprotein of  
 17 similar hydrophobic or antigenic character to that of  
 18 HCV-1.

19 So do I have to do it?

20 MR. RABINOWITZ: Q. Well, let's take  
 21 them -- and then it also says:

22 "...and the presence of co-linear  
 23 peptide sequences that are conserved  
 24 with HCV1."

25

1 Right?  
 2 A. Right.  
 3 Q. Okay, let's take them one by one.  
 4 An open reading frame of approximately 9,000  
 5 nucleotides to approximately 12,000 nucleotides.  
 6 What does "approximately 9,000 nucleotides"  
 7 mean?

8 MR. GRECO: Objection.  
 9 THE WITNESS: It's just English.  
 10 MR. RABINOWITZ: Q. Does that mean plus or  
 11 minus 25% or 50%, or how much variation is  
 12 "approximately"?

13 A. No, don't ask me that kind of question. I  
 14 don't know. It's approximate. It's English defined  
 15 here. So don't ask me to pin down. I could not answer  
 16 your question.

17 Q. And would that be the same if I asked you  
 18 "approximately 12,000 nucleotides" --

19 A. Oh, yes. I will say yes, I could not  
 20 answer.

21 Q. What is a polyprotein similar in size to  
 22 that of HCV-1? What does that mean?

23 MR. GRECO: Objection to the form.  
 24 THE WITNESS: That means the gene

25

1 organization encoded a different gene, and that gene  
 2 could be approximate, could be longer or could be  
 3 shorter.

4 MR. RABINOWITZ: Q. What does "similar in  
 5 size" mean? Again, how similar does it need to be?

6 MR. GRECO: Objection.

7 THE WITNESS: As we discover in this  
 8 patent, we are dealing with RNA virus. RNA virus tend  
 9 to mutate. There is no proof reading for this virus.

10 So even one virus infect you, if I isolate  
 11 the virus from you, you are going to -- we are going to  
 12 see thousand different kind of sequence.

13 So that is how we say, okay, approximate.  
 14 So I cannot tell you exact number. Few amino acid, I  
 15 could not tell.

16 MR. RABINOWITZ: Q. Do you know what the  
 17 size is of the HCV-1 polyprotein?

18 A. This is about 3,000 amino acid.

19 Q. 3,000 amino acids?

20 A. Right.

21 Q. So based on that, are you able to give me  
 22 any boundaries for how similar -- how long or short a  
 23 protein -- a polyprotein would be that was similar in  
 24 size to the one of HCV-1?

25

1 A. No, I cannot.

2 Q. Okay. The next one says, an encoded protein  
 3 of similar hydrophobic and/or antigenic character to  
 4 that of HCV-1.

5 What does it mean, "similar hydrophobic  
 6 character"?

7 MR. GRECO: Objection.

8 THE WITNESS: It's hydrophobicity profile  
 9 of the polyprotein.

10 MR. RABINOWITZ: Q. And how does one  
 11 determine whether something is similar to, in  
 12 hydrophobicity, to HCV-1 polyprotein?

13 A. You just run the computer program with your  
 14 amino acid sequence, and then you find out the  
 15 hydrophobicity profile and you can compare one isolate  
 16 from other isolate, do you see the very similar  
 17 profile.

18 Q. Are there numerical scores for similarity?

19 A. No numerical score for hydrophobicity --  
 20 hydrophobicity.

21 Q. Is that the kind of thing one has to compare  
 22 by eye?

23 A. No, you can put on the computer, and then it  
 24 will draw the graph for you.

1 Q. And do you have to compare the two graphs by  
 2 eye to see how similar they are, or are there  
 3 algorithms for determining the --  
 4 A. You can decide by your eye. You can tell by  
 5 your eye, but if you are fancy, you can go into the  
 6 computer to tell you.

7 Q. So are there computer algorithms for  
 8 measuring the similarity or dissimilarity of  
 9 hydrophobicity of different proteins?

10 A. Yes.

11 Q. Were -- in 1990, were there such programs  
 12 available?

13 A. I think so, yes.

14 Q. Were there many different programs?

15 A. That, I don't know.

16 Q. And what's the meaning of "an encoded  
 17 polyprotein of similar antigenic character to that of  
 18 HCV1"?

19 A. That, as I read this, if you express the  
 20 protein, the protein will pick up the antibody against  
 21 HCV-1.

22 Q. Which antibody is that?

23 A. The antibody against HCV-1 will react with  
 24 your tentative antigen. If you isolate -- when you

25

1 isolate, you express in *E. coli* yeast or mammalian  
 2 cell, get the protein out, ask very simple question.  
 3 Does this protein react with patient infected with  
 4 hepatitis C, type 1? So is there any cross-reaction.

5 Q. So you'd rely on samples of -- on serum  
 6 samples from patients to determine similarity?

7 A. Not necessarily patient. You can get rabbit  
 8 serum or goat serum, if you inject HCV-1 antigen into  
 9 the animal.

10 Q. So if you have a candidate virus and you  
 11 want to see whether its encoded polyprotein has similar  
 12 antigenic character, you would express the polyprotein,  
 13 and test it with a serum, say a rabbit serum, against  
 14 HCV-1 to see whether the serum binds?

15 A. Right.

16 Q. And if the serum binds, that would show that  
 17 the polyprotein has similar antigenic character?

18 A. Yes.

19 Q. So are you saying that any cross-reactivity  
 20 between the polyprotein and the HCV-1 polyprotein shows  
 21 similar antigenic character?

22 MR. GRECO: Object to the form.

23 THE WITNESS: So can you read back?  
 24 (Record read.)

25

1 THE WITNESS: Your question is too broad  
 2 for me to answer.

3 MR. RABINOWITZ: Q. In what respect is it  
 4 too broad?

5 A. Because you try to say cross-react is  
 6 absolute number?

7 Let me answer differently. All immunoassay  
 8 used worldwide is based on hepatitis C, prototype 1.  
 9 And they perform very, very well. There's no instance  
 10 of non A, non B hepatitis in this country and in Japan  
 11 and Europe. And if you isolate in here, in Europe, in  
 12 Japan, there's a different isolate.

13 So what I try to answer intellectually is  
 14 there is a cross-reaction.

15 So you can express the other isolate into  
 16 the protein and ask question, say, that's an antibody  
 17 against HCV-1 cross-react. And then alternative is  
 18 patient infected with, select, say, genotype 2  
 19 cross-react with protein of HCV-1. That is another way  
 20 to do it. And the answer is, yes, I will say both will  
 21 react.

22 Q. Okay. Now, what I'm trying to clarify is,  
 23 when the patent says "similar antigenic character" --

24 A. Right.

1 Q. -- does that mean that you only -- that you  
 2 need only have, say, one antiserum that recognizes both  
 3 proteins, or must many different antisera recognize  
 4 both proteins?

5 MR. GRECO: Objection to the form.

6 THE WITNESS: You are dealing with a  
 7 polyclonal antibody here. Right? So the antibody only  
 8 recognize five amino acid.

9 So if the antibody against this five amino  
 10 acid -- against this five amino acid, what are you  
 11 going to say?

12 So, I don't know, I think that is -- I try  
 13 to answer it, say most or almost all the isolate will  
 14 tend to have very similar protein. And if infected in  
 15 the patient, we are still making the same kind of  
 16 antibody, that's why when we use the type 1 HCV, the  
 17 common antigen will pick up all the different isolate  
 18 in the world.

19 So I think that is the best I can answer to  
 20 you.

21 MR. RABINOWITZ: Q. Isn't it true that  
 22 hepatitis C virus shares some antigenic determinants  
 23 with some Flaviviruses?

24 A. You consider Dengue is Flavivirus or no?

25

1 Q. I'm willing to go with your  
 2 characterization. Do you consider Dengue a Flavivirus?  
 3 A. We tested very early on. We get a sample  
 4 from Trinidad, which is heavily infected with Dengue.  
 5 We didn't see any cross-reaction.

6 But I will not say absolute. There's no  
 7 such thing in the test as a zero and a something. We  
 8 are not dealing with computer here. So what I try to  
 9 say is statistic.

10 Q. But are you aware of any cross-react --  
 11 A. Our test is doing very well worldwide, so if  
 12 there's a cross-reaction, our test will be rejected.

13 Q. I'm not confining it to your tests. I'm  
 14 talking about considering all the antigens on HCV and  
 15 all the antigens on Flaviviruses, is there any common  
 16 antigen between HCV and any other Flavivirus that  
 17 you're aware of?

18 A. Well, that -- the best method is  
 19 epidemiology. If the test is used in million, million  
 20 people, what else you can get best example?

21 So maybe we are coming to different place,  
 22 so I don't know how to answer your question.

23 Q. Dr. Kuo, I'm not confining my question to  
 24 your test. Isn't it true that your test measures --

25

1 How many different HCV antigens does your  
 2 test measure?

3 MR. GRECO: Objection to the form.  
 4 THE WITNESS: No, we are measuring  
 5 antibody.

6 MR. RABINOWITZ: Q. Antibodies to how many  
 7 different antigens in HCV?

8 A. We use a core, and there's three, and  
 9 there's four, and it end at five.

10 Q. Four antigens?

11 A. Yes.

12 Q. Are there -- are you aware of any epitopes  
 13 that are shared or any antigenic determinants that are  
 14 shared between HCV and any Flavivirus?

15 A. I don't -- I'm not aware of that.

16 Q. Are you aware of any epitopes that are  
 17 shared between HCV and any other virus at all?

18 A. That is, again, you can ask "any," that is  
 19 very difficult question for me to answer. So give me  
 20 some kind of number.

21 So the tests, there is no such thing as  
 22 absolute here. It's all statistic. So if you  
 23 run million tests, how many do you see? So I cannot  
 24 say, okay, it's absolutely zero. I cannot tell you  
 25

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190

1 that.

2 So give me example and then I will tell you.

3 Q. So your answer is that you are not, as you  
 4 sit here today, you are not aware of any antigenic  
 5 determinants that are found both in HCV and in any  
 6 other virus?

7 A. I didn't say that. I think all the tests  
 8 will have some false positive, but we do pick up the  
 9 hepatitis C. That is the most important here.

10 The test is specific for C, and then we  
 11 don't say there is no false positive.

12 There's no test that is absolutely --

13 Q. What sort of thing causes false positives?

14 A. That depend on what kind of disease. Could  
 15 be anything.

16 Q. Are there certain types of viruses that  
 17 cause false positive results?

18 A. I don't know. We don't know.

19 If you want me to give you example, there is  
 20 Kansas City. There's a nun donated blood for more than  
 21 ten years, didn't cause any hepatitis in the recipient.

22 When we run the tests, we see hepatitis C,  
 23 first generation, C-100. We pick up the sample.

24 So I say no, this is not hepatitis C because

25

1 the most important is the recipient didn't develop the  
 2 disease. How come the nun get the antibody against --  
 3 actually, we narrow it down to 5-1-1 region. We don't  
 4 know.

5 We are dealing with heterogeneous  
 6 population. We are not dealing with homogeneous  
 7 population here.

8 Q. And so you're not aware of what the nun was  
 9 exposed to that caused antibodies that recognized  
 10 5-1-1?

11 A. No.

12 MR. RABINOWITZ: Okay. I think this is  
 13 probably a good time for a break.

14 THE VIDEOGRAPHER: Going off record. Time  
 15 now is 3:04.

16 (Recess.)

17 THE VIDEOGRAPHER: Going back on record.  
 18 Time now is 3:23.

19 MR. RABINOWITZ: Q. Dr. Kuo, let me direct  
 20 your attention once again to Exhibit 200, the '596  
 21 patent, and again to Column 8, towards the end,  
 22 Line 12. It refers to the presence of co-linear  
 23 peptide sequences that are conserved with HCV-1.

24 Would you explain what that means.

25

1 A. So it's linear peptide sequence conserved  
2 with hepatitis C-1.

3 Q. What are co-linear peptide sequences?

4 A. It's just the primary amino acid sequence.  
5 Q. And what does the term "co-linear" convey?  
6 A. That, I don't know. I didn't use that in  
7 the work, so I don't know.

8 Q. Would you agree that that refers to  
9 sequences or motifs that are found in different parts  
10 of different regions of a polypeptide?

11 MR. GRECO: Objection.

12 THE WITNESS: No, I don't know. I could  
13 not answer your question.

14 MR. RABINOWITZ: Okay, thank you.  
15 Q. Now, going back to the various criteria that  
16 we have been discussing, an ORF of approximately 9,000  
17 nucleotides to approximately 12,000 nucleotides, a  
18 polyprotein similar in size to that of HCV-1 encoded  
19 polyprotein of similar hydrophobic character,  
20 encoded --

21 (Reporter interruption.)

22 MR. RABINOWITZ: Q. -- polyprotein of  
23 similar antigenic character to HCV-1, presence of  
24 co-linear peptide sequences conserved with HCV-1, those

25

1 are five different criteria.

2 Must a candidate virus possess all of those  
3 to qualify as an HCV-1?

4 MR. GRECO: Object to the form.

5 THE WITNESS: Personally, I don't think  
6 so. I think that is the criteria you can use.

7 MR. RABINOWITZ: Q. Are these just examples  
8 of criteria?

9 A. What do you mean by "examples of criteria"?

10 Q. Well, I see that the patent says, "These  
11 would be defined as HCV according to various criteria  
12 such as, for example," and then it mentions all of  
13 those.

14 A. Yes, already described here, "for example."

15 Q. So these are just examples. There are other  
16 criteria one can use instead?

17 MR. GRECO: Object to the form.

18 THE WITNESS: Maybe.

19 MR. RABINOWITZ: Q. What would those other  
20 criteria be?

21 A. That, I don't know.

22 Q. As far as you're aware, are other criteria  
23 spelled out in this patent for classifying a virus as  
24 an HCV-1?

25

1 MR. GRECO: Objection to form.  
2 THE WITNESS: And this paragraph already  
3 mentioned this is "defined as HCV according to various  
4 criteria, such as."

5 So we already describe here.

6 MR. RABINOWITZ: Q. They describe some, but  
7 there are others as well. Right? These are for  
8 example.

9 A. There could be.

10 Q. And I'm asking whether you can point to any  
11 other part of the patent that lists other criteria.

12 A. I didn't read the patent. I just read now,  
13 so I could not tell you. I could not answer.

14 Q. Okay. Let's go to the next paragraph in  
15 Column 8, where it says:

16 "All HCV isolates encode at least  
17 one epitope which is immunologically  
18 identifiable (i.e., immunologically  
19 cross-reactive) with an epitope encoded  
20 in the HCV cDNAs described herein."

21 Firstly, do you agree that this is a  
22 criterion that an isolate needs to satisfy to be  
23 classified as an HCV?

24 A. But already described in previous paragraph  
25

1 in antigenic character.

2 Q. But I'm asking you, is it necessary for a  
3 virus to encode at least one epitope which is  
4 immunologically identifiable with an epitope encoded in  
5 the HCV cDNAs described in this patent in order to  
6 qualify it as an HCV?

7 A. It's just for patent say here.

8 Q. That's what the patent says. Right?

9 A. Yes.

10 Q. And so if a candidate virus does not encode  
11 at least one epitope which is immunologically  
12 cross-reactive with an epitope encoded in the HCV cDNAs  
13 in the patent, then it would not be an HCV. Right?

14 A. No, your question is too vague. I could not  
15 answer.

16 So you will try to tell me if you find some  
17 negative result, doesn't react with one of the HCV-1  
18 protein, and then you will say, okay, this is not HCV,  
19 I don't accept that.

20 Q. Well, then what does it mean when it says  
21 all HCV isolates encode at least one epitope which is  
22 immunologically identifiable --

23 A. That is English. It say this one. You have  
24 to look a lot of the epitope.



1 coexist with C in our blood supply? If they exist, our  
 2 tests is doing very well. So we didn't have too much  
 3 problem.

4 Q. Now, I'm going to direct your attention to  
 5 the next paragraph in Column 8, which says:

6 "HCV strains and isolates are  
 7 evolutionarily related. Therefore, it  
 8 is expected that the overall homology  
 9 of the genomes at the nucleotide level  
 10 may be about 40% or greater..."

11 And then the sentence continues:

12 "...probably will be about 50% or  
 13 greater," and so on.

14 Just read that entire sentence to yourself.

15 MR. GRECO: Maybe read the whole  
 16 paragraph.

17 MR. RABINOWITZ: And anything else you want  
 18 to read to yourself, too, and let me know when you're  
 19 finished doing that.

20 THE WITNESS: Yes.

21 MR. RABINOWITZ: Q. Is there a minimum  
 22 overall homology of the genome at the nucleotide level  
 23 that a candidate virus must satisfy in order to be  
 24 classified as an HCV?

25

1 A. It's already described in this paragraph.  
 2 Q. Well, the paragraph says -- isn't it true  
 3 the paragraph says it is expected that the overall  
 4 homology may be about 40% or greater?

5 A. Yes.

6 Q. It doesn't say that it must be 40% or  
 7 greater.

8 MR. GRECO: So what's the question now?

9 MR. RABINOWITZ: Q. It's true, it does not  
 10 say that it must be 40% or greater. Right?

11 A. Yeah, that says may be.

12 Q. May be. Does that mean that a candidate  
 13 virus must be at least 40% homologous at nucleotide  
 14 level to qualify as HCV?

15 A. No, it says just may be, didn't say must be.

16 Q. So a candidate virus can qualify as an HCV  
 17 even if it doesn't have at least 40% overall homology  
 18 at nucleotide level. Right?

19 A. But we just set up the criteria in the first  
 20 paragraph of Column 8.

21 Q. I'm asking about the criterion of overall  
 22 homology at nucleotide level. We've not discussed that  
 23 before.

24 My question to you is this. If it satisfies

25

201

202

1 various other criteria, it need not be at least 40%  
 2 homologous at nucleotide level overall to HCV-1 to be  
 3 classified as an HCV. Right?

4 A. In here it just says may be about 40% or  
 5 greater.

6 Q. So that's not a necessary qualification to  
 7 satisfy the definition of HCV. Right?

8 A. From nucleotide sequence, that is true.

9 Q. Right. So just to make sure I understand  
 10 your answer correctly, it's not a requirement for  
 11 classification as HCV that the candidate virus must  
 12 necessarily have at least 40% overall homology at the  
 13 nucleotide level. Is that right?

14 A. But are you going to abandon criteria in the  
 15 first paragraph of Column 8?

16 Q. I'm talking about in addition to whatever  
 17 other criteria apply. I'm just asking whether at least  
 18 40% homology of nucleotide level --

19 A. But my answer is you have to satisfy the  
 20 first paragraph criteria, then this nucleotide sequence  
 21 is separate.

22 Q. Good, and so my question --

23 A. It may be 40%.

24 Q. So my question to you is, if the first

25

1 paragraph of Column 8 is satisfied, then it is not  
 2 necessary for a virus to have at least 40% homology at  
 3 nucleotide level to qualify as an HCV. Right?

4 A. May be 40% or greater homology. That is  
 5 what it say here.

6 Q. Could it be less than 40%?

7 A. That is your assumption. We just say it may  
 8 be 40% or greater, but if you want to say 40% or less,  
 9 that is your assumption here.

10 Q. Well, that's why I'm asking you whether that  
 11 is correct. Is that a correct assumption?

12 A. But we didn't say that in here.

13 Q. What you said is that the overall homology  
 14 may be about 40% or greater.

15 A. Yes.

16 Q. I'm asking you, is 40% homology a  
 17 prerequisite in order to classify a virus as HCV?

18 MR. GRECO: Objection to the form.

19 THE WITNESS: I could not answer your  
 20 question. We say, okay, should be greater than 40%.  
 21 And then you want to make an assumption is under 40%,  
 22 ask my opinion.

23 We didn't say anything about under 40%, so  
 24 it's difficult for me to say anything.

25

203

204

1           You assume something here, and we didn't say  
 2 any -- 40% -- if we say -- if 40% is not HCV, I will  
 3 say, yes, we say that, but we didn't say. When we  
 4 didn't say anything, we cannot say we say something.

5           MR. RABINOWITZ: Can I ask the reporter to  
 6 read back the last two sentences of that answer.

7           (Record read.)

8           MR. RABINOWITZ: Q. So do you agree that  
 9 the patent does not say that the overall homology at  
 10 the nucleotide level must be 40% or greater?

11           MR. GRECO:     Object to the form.

12           THE WITNESS:    May be 40% or greater, that  
 13 is said in the patent.

14           MR. RABINOWITZ: Q. The patent does not say  
 15 it must be 40% or greater, right?

16           A.            In a word, that's true, but I don't know in  
 17 legal explanation.

18           Q.            Let me go back to the preceding paragraph,  
 19 which discusses epitopes of HCV isolates.

20           Does the patent say that all HCV isolates  
 21 have at least one epitope in common with all other HCV  
 22 isolates?

23           MR. GRECO:    Objection to the form.

24           THE WITNESS:    No. All HCV isolate encode

25

1           at this one epitope which is immunologically  
 2 identifiable.

3           MR. RABINOWITZ: Q. Does that mean with --  
 4 A.           With epitope encoded in HCV cDNA described  
 5 herein.

6           Q.            What my question is, is there at least one  
 7 epitope that is common to all HCV isolates, is that  
 8 what that sentence means?

9           A.            No, I don't think that is what the sentence  
 10 means.

11           Q.            Does the sentence mean that HCV can share,  
 12 call it epitope 1 with a particular HCV isolate, and  
 13 may share epitope 2 with a different HCV isolate, and  
 14 share epitope 3 with yet a third HCV isolate, but not  
 15 necessarily the same one epitope with all of them?

16           MR. GRECO:    Object to the form.

17           THE WITNESS:    For example, if there's a  
 18 hundred epitope of hepatitis C, type 1, if you want to  
 19 say this unknown hepatitis C, the question is, do they  
 20 have one of the epitope similar to the HCV-1?

21           If the answer is yes, this one similar to  
 22 the type 1, we'll claim that it's hepatitis C.

23           MR. RABINOWITZ: Q. And the second isolate  
 24 may share a different epitope with HCV-1?

25

1           A.            May be same, may be different.  
 2 Q.            So it's not required that they all share the  
 3 same, at least one epitope in common with each other.  
 4 Right?

5           A.            That is my interpretation.

6           Q.            Good, thank you. Let me direct your  
 7 attention back to the claims of the '596 patent.  
 8 Actually, we're going to move on to Column 55,  
 9 Claim 22.

10           Would you read that claim over, and I'm  
 11 going to focus on the phrase "a unique nucleotide  
 12 residue sequence."

13           What does that mean, "a unique nucleotide  
 14 residue sequence"?

15           MR. GRECO:    Object to the form.

16           THE WITNESS:    It's just unique sequence.

17           MR. RABINOWITZ: Q. What does that mean,  
 18 "unique"?

19           A.            There's only one sequence, all right?

20           Q.            Do you mean the sequence is only found in  
 21 HCV and not other viruses?

22           A.            No, didn't say that.

23           Q.            Well, then what does "unique" mean?

24           A.            If you dissect 9kb HCV-1 sequence, so

25

1           certain region is 5 or 10 nucleotide, it's only found  
 2 in hepatitis C. So that is --

3           Q.            And not found in anything other than your  
 4 hepatitis C?

5           A.            But what I try to say is not particular  
 6 region. You have to look all of them.

7           Q.            So that's referring to a particular region  
 8 of hepatitis C that's --

9           A.            No, I didn't say particular region.

10           MR. RABINOWITZ: Dr. Kuo, I'm going to ask  
 11 you let me finish my question before you answer. I  
 12 know sometimes it's difficult, but I will ask you to do  
 13 that.

14           Q.            My question is, it says:

15           "....a contiguous sequence of at least  
 16 10 nucleotides fully complementary to a  
 17 unique nucleotide residue sequence in  
 18 either strand of the nucleotide residue  
 19 sequence depicted in Figure 1."

20           Does that mean that there's a sequence of at  
 21 least 10 nucleotides in -- depicted in Figure 1 that's  
 22 found only in HCV?

23           MR. GRECO:    Objection.

24           THE WITNESS:    You have to work through

25

1 all the genome. Make all the 10, 10-mer, and then see,  
 2 okay, this is unique to the hepatitis C.

3 MR. RABINOWITZ: Q. How do you tell whether  
 4 it's unique to hepatitis C?

5 A. It's only found in hepatitis C.

6 Q. What do you have to compare it with?

7 A. Compare with all the isolates. So you give  
 8 me a hypothetical region.

9 Example. Okay, if you have a sequence,  
 10 okay, similar or unique -- similar to type 1, am I  
 11 going to call that hepatitis C?

12 I say, well, you have to look all the  
 13 sequence. We didn't give you the particular sequence  
 14 here, so you have to compare all the 10 nucleotide.

15 Q. Let me ask you this. If I provide you with  
 16 an oligonucleotide that is perfectly complementary to,  
 17 let's choose a sequence of HCV, let's say nucleotides  
 18 100 through 110 as depicted in Figure 1, and I ask you,  
 19 "Is such an oligonucleotide fully complementary to a  
 20 unique nucleotide residue sequence in either strand of  
 21 Figure 1," how would you determine whether that  
 22 particular oligonucleotide satisfies that criterion of  
 23 uniqueness?

24 MR. GRECO: Sorry. Objection.

25

1 THE WITNESS: So you just pick up  
 2 randomly 10 polynucleotide, is homology to the HCV-1?  
 3 MR. RABINOWITZ: Q. It's perfectly  
 4 complementary to HCV-1. But my question is, what tests  
 5 do you need to do to see whether it fulfills this  
 6 claim, satisfies this claim?

7 MR. GRECO: Objection.

8 THE WITNESS: And where you get the  
 9 sequence? Is it synthesized randomly, or you pick up  
 10 the sequence from isolate?

11 MR. RABINOWITZ: Q. Let's say that it's  
 12 synthesized randomly. What tests do you need to do?

13 A. 10 oligonucleotides? We didn't claim that.

14 That is not virus.

15 Q. I beg your pardon?

16 A. That oligonucleotide is not virus. You just  
 17 synthesized it.

18 Q. Well, let's take a look at Claim 22. It  
 19 talks about the purified preparation of Claim 1.

20 If I look back at Claim 1, Claim 1 is  
 21 directed to a purified preparation of an  
 22 oligonucleotide that satisfies certain limitations.

23 And then it says, wherein the  
 24 oligonucleotide comprises a contiguous sequence of at  
 25

1 least 10 nucleotides fully complementary to a unique  
 2 nucleotide residue sequence in either strand of the  
 3 nucleotide residue sequence depicted in Figure 1.

4 Do you agree that Claim 22 is directed to a  
 5 preparation of an oligonucleotide?

6 MR. GRECO: Objection to the form.

7 THE WITNESS: Yes.

8 MR. RABINOWITZ: Q. It can be a synthetic  
 9 oligonucleotide --

10 A. But you need Figure 1 to synthesize it. You  
 11 cannot randomly synthesize it.

12 Q. Okay, now here is my example. Based on  
 13 Figure 1, I've synthesized an oligonucleotide that is  
 14 perfectly complementary to nucleotides 100 through 110  
 15 in Figure 1.

16 How do I determine whether such a  
 17 preparation of an oligonucleotide satisfies the  
 18 requirements of Claim 22 as far as uniqueness is  
 19 concerned?

20 MR. GRECO: Objection.

21 THE WITNESS: But you've already used the  
 22 sequence in Figure 1 to synthesize the oligonucleotide.  
 23 So I don't understand your question here.

24 MR. RABINOWITZ: Q. Will such an

1 oligonucleotide preparation be complementary to a  
 2 unique nucleotide sequence?

3 A. In a particular case, yes. But you have to  
 4 start it. You cannot just pick up randomly.

5 Q. So I'm trying to find out, is anything  
 6 that's perfectly complementary to at least 10  
 7 nucleotides of Figure 1 going to be unique within the  
 8 meaning of this claim?

9 MR. GRECO: Objection.

10 THE WITNESS: If you synthesize 10  
 11 nucleotide randomly without look at the sequence in  
 12 Figure 1, I will say no.

13 MR. RABINOWITZ: Q. No, Dr. Kuo, that is  
 14 not my question.

15 I'm saying if I choose an oligo that's  
 16 identical to any randomly chosen 10-mer in Figure 1,  
 17 will that necessarily satisfy the requirement of  
 18 uniqueness in Claim 22?

19 MR. GRECO: Objection.

20 THE WITNESS: I still cannot understand  
 21 your question.

22 MR. RABINOWITZ: Let me come at it another  
 23 way.

24 Q. What is the meaning of "unique" in Claim 22

25

1 as you understand it?

2 MR. GRECO: Objection.

3 THE WITNESS: As I understand, that is  
4 use the Figure 1 sequence to make that 10 nucleotide.

5 MR. RABINOWITZ: Q. That's what "unique"  
6 means?

7 A. As I understand, yes.

8 Q. Okay. Let me direct you to Column 9,  
9 Line 6. The two sentences beginning on Line 6. Of  
10 course, read anything else around it that you need to  
11 for context.

12 Please let me know when you've finished  
13 looking.

14 A. Yes.

15 Q. So it says:

16 "...the sequence of the region from  
17 which the polynucleotide is derived is  
18 homologous to or complementary to a  
19 sequence which is unique to an HCV  
20 genome. More preferably, the derived  
21 sequence is homologous or complementary  
22 to a sequence that is unique to all or  
23 to a majority of HCV isolates."

24 And then it goes on to describe various

25

1 techniques for determining whether a sequence is unique  
2 to the HCV genome.

3 Does that help clarify what the term  
4 "unique" means --

5 MR. GRECO: Objection.

6 MR. RABINOWITZ: Q. -- in Claim 22?

7 A. It gives example. Several way to do it.  
8 Q. So it says the sequence can be compared to  
9 known sequences of other viral agents.

10 A. Right.

11 Q. Why would one make that comparison in  
12 testing for uniqueness?

13 A. So what is your question? I confused here.

14 Q. My question is, doesn't this describe that a  
15 unique sequence must be one that's not found in other  
16 organisms besides hepatitis C virus?

17 MR. GRECO: Objection to the form.

18 THE WITNESS: Yes, I see that is one  
19 definition.

20 MR. RABINOWITZ: Q. Take a look at, I think  
21 it's Line 13 in Column 9. It says:

22 "For example, the sequence can be  
23 compared to sequences in databanks,  
24 e.g., Genebank, to determine whether it  
25

1 is present in the uninfected host or  
2 other organisms."

3 Do you see that?

4 A. Yes.

5 Q. Don't you agree, if the sequence is present  
6 in the uninfected host, it wouldn't be unique to HCV,  
7 would it?

8 A. And that, we will not use that as a primer.

9 Q. So a unique sequence must be present in HCV,  
10 but not in the uninfected host. Right?

11 MR. GRECO: Objection to the form.

12 THE WITNESS: That is when you want to  
13 use that to develop the test. So it's a different  
14 question here.

15 I keep saying, if you look hard enough,  
16 maybe you will see the homology between HCV virus and  
17 maybe virus from alligator or something, but we are  
18 dealing with a human disease here.

19 So if we want to diagnose human disease, we  
20 want to use HCV sequence that is unique to HCV, is not  
21 found in the host cell or not found in other virus. So  
22 that is our definition.

23 MR. RABINOWITZ: Q. Okay. So unique means  
24 it's not found in the host cells or in other viruses.

1 Right?

2 MR. GRECO: Object to the form.

3 THE WITNESS: To develop the test. It's  
4 just for practical meaning.

5 MR. RABINOWITZ: Q. So I'm not sure whether  
6 you are agreeing with me that a unique sequence means a  
7 sequence that's found in HCV but not in the host or in  
8 other viruses.

9 A. The oligonucleotide is used for other  
10 purpose.

11 For that purpose, we have to use this unique  
12 sequence for the HCV, not for other virus. So that is  
13 for the practical purpose. We are not talking about  
14 theoretical here.

15 Q. I just want to go back for a moment to  
16 Column 8, the paragraph beginning Line 16 concerning  
17 epitopes.

18 Does the patent provide or describe any  
19 reference serum that can be used to determine whether a  
20 candidate virus shares an epitope with HCV -- HCV-1?

21 MR. GRECO: Objection.

22 THE WITNESS: So can you read back the  
23 question?

24 (Record read.)

1           THE WITNESS:    I don't understand your  
2 question at all, sorry.  Maybe you have to rephrase it.

3           MR. RABINOWITZ:  Okay, let me try it again.

4           Q.        Are there standard sera that you can use in  
5 order to classify a candidate virus as HCV or not HCV?

6           A.        No, there is no standard serum.

7           Q.        No standard serum.  Does the patent provide  
8 a particular serum as a reference serum to use in  
9 determining whether a newly isolated virus shares a  
10 common epitope with the cDNAs described in the patient?

11          A.        I still don't understand your question.

12          What do you want to get to?

13          For example, like if you want to get the HCV  
14 isolate, the first thing is use our immunoassay to pick  
15 up is there an antibody.  Then if there's antibody,  
16 then try to sequence it, try to clone it.

17          So you try to say, okay, if there's a -- we  
18 don't have a panel set up by reference lab or  
19 something.  If you pass this panel, then you say  
20 hepatitis C.  If you don't, it's not.

21          No, we don't have that.

22          Q.        And you don't have a panel defined in the  
23 patent itself?

24          A.        No, but in here it is described different.

25

1           That's why I'm confused with your question here.

2           Encoded at least one epitope which is  
3 immunologically identifiable.  So that is the sentence,  
4 with the epitope encoded in HCV cDNA library described  
5 here.

6           Q.        Now, in order to test whether it encodes at  
7 least one epitope which is immunologically  
8 identifiable, you need to use at least one antiserum to  
9 test that.  Right?

10          A.        Right.

11          Q.        Or a monoclonal antibody.  Right?

12          A.        Right.

13          Q.        Does the patent tell you which monoclonal  
14 antibodies you can use or which sera you can use to do  
15 that testing?

16          MR. GRECO:    Objection to the form.

17          THE WITNESS:  This one percent of the  
18 total population in the world infected with  
19 hepatitis C.  There's plenty of serum you can use, so I  
20 don't know what is -- why we have to provide an  
21 antiserum to identify it.

22          MR. RABINOWITZ:  Q.  Is that why the patent  
23 doesn't specify a particular serum or antibody to use?

24          A.        It just tell you, say, okay, describe what

25

1          is our territory.  So we say encode at least one  
2 epitope which is immunologically identifiable.  And  
3 that is -- it's not particular technology.  You can use  
4 different way to do it.

5          Q.        Okay.  And so in order to look at the  
6 epitope encoded in the HCV cDNAs described in the  
7 patent, you'd have to express the cDNAs and then make  
8 antibodies against them, wouldn't you?

9          A.        Not necessarily.

10         MR. GRECO:    Object to the form.

11         Go ahead.

12         MR. RABINOWITZ:  Q.  What would you have to  
13 do?

14         A.        You can screen the human serum sample to  
15 find out is this serum react with this protein or not.  
16 Once it react, this is this antibody.

17         Q.        If you pick up -- are you saying that immune  
18 serum is specific for HCV encoded epitopes?

19         A.        No, I didn't say that.

20         Q.        Isn't it true that serum from patients with  
21 HCV would contain antibodies to things that are not  
22 encoded in the cDNAs described in the patent?

23         A.        No, I didn't say that.  What I say --  
24 You give me the example, say if you clone

1          the cDNA, express the protein.  All right?

2          I say once you have that protein, you can  
3 identify the patient serum which will contain antibody  
4 against that protein.  If necessary, you can phage or  
5 purify that antibody, and become a mono-specific serum.

6          Q.        I'm interested in the first step of what you  
7 said.  You said you clone the cDNA and then you express  
8 it.

9          A.        Right.

10         Q.        Does it matter what cells you express the  
11 protein in?

12         A.        Of course it matter, yes.

13         Q.        What difference does it make what cells you  
14 express the protein in?

15         A.        Well, you express in -- it depend on which  
16 gene you want to express.  You want to express E1, E2,  
17 it's a glycosylate.  You better express in mammalian  
18 cell.

19         Q.        What happens if you express it in yeast?

20         A.        In yeast, it's non-glycosylate.

21         Q.        In yeast it's not glycosylate?

22         A.        Internal is not glycosylate.

23         Q.        If you express it in bacteria, will it be  
24 glycosylate?

1 A. No, of course not.  
 2 Q. Will all mammalian cells glycosylate it the  
 3 same?  
 4 A. We use particular ones, CHO cells. C-H-O  
 5 cells will glycosylate same as human.  
 6 Q. What other cells could you use instead of  
 7 CHO cells?  
 8 A. Why you want to use other cell?  
 9 Q. I'm just asking what other cells you could  
 10 use.  
 11 A. No, you can use other different cell, like  
 12 baculovirus system.  
 13 Q. What about BHK cells, could you use those?  
 14 A. If you want. That is a personal choice.  
 15 There's no reason you use, but CHO cell has been used  
 16 in common.  
 17 Q. Will BHK cells glycosylate cDNAs in the same  
 18 way as CHO cells?  
 19 A. That, I cannot tell you. I don't know.  
 20 Q. Would it make a difference to the epitope if  
 21 the glycosylation was different?  
 22 A. Maybe.  
 23 Q. Would it make a difference to the epitope if  
 24 the glycosylation was absent?  
 25

1 MR. RABINOWITZ: Q. So Exhibit 202,  
 2 Page 11. The first bullet point. Do you see there, it  
 3 says:  
 4 "...a 'purified preparation' is defined  
 5 in the '714 application at page 15,  
 6 lines 8 to 17."  
 7 Do you see that?  
 8 A. Yes.  
 9 Q. Would you turn to Page 15, Lines 8 to 17 of  
 10 the '714 application, Exhibit 203.  
 11 A. Yes.  
 12 Q. Do you agree that a purified preparation of  
 13 viral polynucleotide refers to a non A, non B virus  
 14 genome or fragment thereof which is essentially free of  
 15 polypeptides with which the viral polynucleotide is  
 16 naturally associated?  
 17 MR. GRECO: Object to the form.  
 18 THE WITNESS: So what is your question?  
 19 MR. RABINOWITZ: Q. Do you agree with that  
 20 definition?  
 21 A. Yes.  
 22 Q. Do you agree that "polynucleotide" in the  
 23 '596 patent means the same thing as "oligonucleotide"?

24 MR. GRECO: Object to the form.

1 A. For some epitope, yes.  
 2 MR. RABINOWITZ: I think it's been about an  
 3 hour since we began. Let's take a short break and then  
 4 maybe we can --  
 5 MR. GRECO: Go for the home stretch.  
 6 MR. RABINOWITZ: -- go for the home stretch.  
 7 THE VIDEOGRAPHER: In the deposition of  
 8 Dr. George Kuo, this marks the end of Videotape 3.  
 9 Going off record, the time now is 4:11.  
 10 (Recess.)  
 11 THE VIDEOGRAPHER: In the deposition of  
 12 Dr. George Kuo, Ph.D., this marks the beginning of  
 13 Videotape 4. Going back on record, the time now is  
 14 4:21.  
 15 MR. RABINOWITZ: Q. Dr. Kuo, let me direct  
 16 your attention for a moment to Exhibit 202. That's the  
 17 amendment dated February 27, 1995.  
 18 And also to Exhibit 203, which is the '714  
 19 application, at Page 15 of that application.  
 20 MR. GRECO: You say 202 and 203.  
 21 This is 203. This is --  
 22 THE WITNESS: 202.  
 23 MR. GRECO: 202 is 202. These two is  
 24 what you need.  
 25

1 answer.

2 MR. RABINOWITZ: Q. Now, with respect to  
 3 Claim 1 of Exhibit 200, which is the '596 patent, do  
 4 you agree that the meaning of "purified preparation" is  
 5 given in Exhibit 203, which is the '714 application,  
 6 Page 15, Lines 8 to 11?

7 MR. GRECO: Objection.

8 THE WITNESS: No. This is -- says,  
 9 purified preparation of viral polynucleotide.

10 And in the Claim 1 is purified preparation  
 11 of an oligonucleotide.

12 MR. RABINOWITZ: Q. Now, take a look at  
 13 Exhibit 202, Page 11, the first bullet point.

14 A. Yes.

15 Q. Do you see it says, "A purified preparation  
 16 of an oligonucleotide"?

17 A. Yes.

18 Q. Is that the same as the text of -- the  
 19 initial text of Claim 1 on Column 52 of the '596  
 20 patent, "A purified preparation of an oligonucleotide"?

21 A. Yes.

22 Q. Okay, let's go back to Exhibit 202. It  
 23 continues. "...a 'purified preparation' is defined in  
 24 the '714 application at page 15, lines 8-17." Right?

25

1 A. All right.

2 Q. So let's go to --

3 So do you agree that the definition of  
 4 "purified preparation" on Page 15, beginning at Line 8,  
 5 applies to the term "purified preparation" in Claim 1  
 6 of the '596 patent?

7 MR. GRECO: Objection.

8 THE WITNESS: Could you read back the  
 9 question, please.

10 (Record read.)

11 THE WITNESS: Yes, that is one way to  
 12 define purified prep of the oligonucleotide.

13 MR. RABINOWITZ: Q. And so "purified  
 14 preparation" in Claim 1 means "a preparation which is  
 15 essentially free of polypeptides with which the viral  
 16 polynucleotide is naturally associated." Correct?

17 MR. GRECO: Objection.

18 THE WITNESS: But they say before that,  
 19 they refer to non A, non B genome or fragment.

20 MR. RABINOWITZ: Q. So that part of the  
 21 definition as well?

22 A. Yeah.

23 Q. So a purified preparation in Claim 1 is a  
 24 purified preparation of a non A, non B virus genome or

25

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1 fragment thereof, which is essentially free of  
 2 polypeptides with which the viral polynucleotide is  
 3 naturally associated?

4 MR. GRECO: Objection.

5 MR. RABINOWITZ: Q. Right?

6 A. Right.

7 Q. Let's go to Exhibit 200, the '596 patent,  
 8 Claim 7.

9 We're finished with Exhibits 202 and 203 for  
 10 the moment.

11 Could you read through Claim 7 and then  
 12 explain to me what the meaning is of "a conserved HCV  
 13 nucleotide sequence."

14 A. So what is your question here?

15 Q. Will you explain to me, please, what the  
 16 term "conserved HCV nucleotide sequence" means?

17 A. That means the sequence is present in most  
 18 of the isolate.

19 Q. The particular sequence is present in --

20 A. Yeah.

21 Q. When you say "most isolates," what do you  
 22 mean by "most isolates"?

23 A. That is just most of the isolate. I didn't  
 24 say 100% of isolate.

1 Q. What percentage would be required for a  
 2 sequence to be conserved?

3 A. I could not tell you the percentage. I say  
 4 this is a relative term.

5 When you say you are conservative, you are  
 6 liberal, can you measure it? No way you can measure  
 7 it.

8 It's the same thing. How can you measure?  
 9 It's just relative.

10 Q. So how would someone be able to determine  
 11 whether a particular sequence, a particular  
 12 oligonucleotide, fell within the scope of Claim 7?

13 Let's say it was within the scope of  
 14 Claim 1, but they wanted to test to see whether it was  
 15 also within the scope of Claim 7. What test would they  
 16 have to do to see whether it qualified as a conserved  
 17 HCV nucleotide sequence?

18 A. You have to compare the sequence.

19 Q. With what?

20 A. With your isolate. So we have HCV, type 1  
 21 sequence here. If you have a new isolate, you compare  
 22 two sequence, say which part is conserve. So that is a  
 23 conserved region.

24 Q. So a conserved region is a region which is

25

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1 exactly present both in HCV-1 and in the new isolate?  
 2 MR. GRECO: Object to the form.  
 3 THE WITNESS: Not exactly. So I say this  
 4 is a relative term.

5 So you can say certain region, like  
 6 nucleocapsid region, with a rate of conserve. So more  
 7 likely we are very similar, only few amino acid will  
 8 change.

9 MR. RABINOWITZ: Q. Where do you draw the  
 10 line between conserved and not conserved?

11 A. We have no line to draw. It's just  
 12 operational. It's practical.

13 You want to develop something, immunoassay.  
 14 Why would you choose hepatitis core as the antigen?  
 15 Because it's a relative conserve. So that is --

16 We cannot say, okay, you have to meet this  
 17 criteria in order to claim it is conserved. No, there  
 18 is no line we can draw.

19 Q. Would you agree that a conserved HCV  
 20 nucleotide sequence means a portion of the genomic  
 21 HCV --

22 (Reporter interruption.)

23 MR. RABINOWITZ: Q. Would you agree that a  
 24 conserved HCV nucleotide sequence means a portion of

25

1 the genomic sequence of HCV that has less genotype to  
 2 genotype variability than the genome as a whole?

3 A. Yes, I agree with that.

4 Q. How do you determine how much --

5 So you need to compare it with the average  
 6 variability of the genome. Right?

7 MR. GRECO: Object to the form.

8 THE WITNESS: Computer sequence.

9 MR. RABINOWITZ: Q. No, in order to --

10 So you compare the variability of the  
 11 particular sequence with the variability of the genome  
 12 as a whole. Is that what you're saying?

13 A. That depend on what you want to do.

14 You're asking me how you define the conserve  
 15 region, and I just say, okay, compare two sequence. If  
 16 there's a sequence very similar or is very -- the  
 17 homology is very high, and then you say that is  
 18 conserved region.

19 That is what I just explained to you.

20 Q. So very high homology?

21 A. I would say yes.

22 Q. Are you talking in the 80 to 90% homology?

23 A. No, I don't say. That depend on how you  
 24 want to do with it. So I don't draw the line.

25

1 Q. You say for some purposes it might need to  
 2 be 80 to 90%?

3 MR. GRECO: Object on form.

4 THE WITNESS: I don't know. As I  
 5 mentioned very, very early, I'm not expert in nucleic  
 6 acid diagnostic or doing this, so I can only give you  
 7 my opinion.

8 MR. RABINOWITZ: Q. So in your opinion,  
 9 would 30 to 40% be enough?

10 A. I'm not --

11 MR. GRECO: Objection.

12 THE WITNESS: I'm not doing it. If my  
 13 hand is not dirty, I don't make any comment.

14 MR. RABINOWITZ: Q. So you can't say where  
 15 one would draw the line?

16 A. I, personally, I don't know how to draw it.  
 17 Someone else may be.

18 Q. Would you take a look at Exhibit 200, which  
 19 is the '596 patent, at Column 18, Line 51, to  
 20 Column 19, Line 5, and read through that to yourself.  
 21 Column 18, Line 51.

22 A. Yes.

23 Q. To Column 19, Line 5.

24 MR. GRECO: Again, that starts in the

1 middle of a paragraph, so why don't you just --  
 2 (Simultaneous dialog.)

3 MR. RABINOWITZ: Read anything in the  
 4 immediate area or elsewhere in the patent that you need  
 5 to.

6 THE WITNESS: Yes.

7 MR. RABINOWITZ: Q. Does that passage tell  
 8 you where to draw the line to determine whether a  
 9 sequence is conserved or not?

10 MR. GRECO: Objection to the form.

11 THE WITNESS: That is describing the  
 12 paragraph, so I have no way to judge. It is written by  
 13 our patent attorney.

14 MR. RABINOWITZ: Q. When you as a scientist  
 15 read that, do you know how to draw the distinction  
 16 between a conserved sequence and a non-conserved  
 17 sequence?

18 A. I just mentioned, I am not the expert in  
 19 nucleic acid biochemistry here, so I could not answer.

20 Q. Okay. Let me draw your attention to the  
 21 same patent, Line 33 (sic), Lines 23 to 32.

22 And, again, read anything that you need for  
 23 context as well.

24 MR. GRECO: Is it Column 33?

25

1 MR. RABINOWITZ: Column 33, Lines 23 to 32.  
 2 THE WITNESS: Okay.  
 3 MR. RABINOWITZ: Q. Does that help you  
 4 determine how much variability is permitted --  
 5 A. No. I still tell you same thing. This is  
 6 done by somebody else, so I am in no position to judge.  
 7 Q. Who did that determination?  
 8 A. I really don't know. You better ask our  
 9 patent attorney. There's so many people on the patents  
 10 here, so.  
 11 Q. Does it not suggest to you that there should  
 12 almost be no variation at all? It talks about  
 13 identical except for one nucleotide.  
 14 MR. GRECO: Objection to the form.  
 15 THE WITNESS: I don't know. As I  
 16 mention, I don't know anything, so how can I answer the  
 17 question?  
 18 MR. RABINOWITZ: Okay.  
 19 Q. Let me take you now to the same patent,  
 20 Column 49, Lines 51 to 56.  
 21 A. Which column?  
 22 Q. Column 49.  
 23 A. 49.  
 24 Q. Lines 51 to 56.  
 25

1 Kuo, George v. 1 Confidential  
 2 MR. GRECO: Objection to the form.  
 3 THE WITNESS: No, I could not answer,  
 4 because this is another nucleic acid question.  
 5 MR. RABINOWITZ: Q. I'm going to ask you to  
 6 look at Column 26 of the '596 patent, Lines 9 to 21.  
 7 That's the paragraph beginning, "It is anticipated."  
 8 A. Okay.  
 9 Q. Does that tell you where to draw the  
 10 distinction between a conserved and a non-conserved  
 11 sequence?  
 12 MR. GRECO: Objection to the form.  
 13 THE WITNESS: This is very long  
 14 paragraph, so you have to separate your question into  
 15 separate, otherwise it's confusing.  
 16 MR. RABINOWITZ: Q. What's confusing about  
 17 it?  
 18 A. Because in the last sentence or the  
 19 paragraph we are mentioning about the Flaviviruses.  
 20 Q. And why is that confusing?  
 21 A. Because I don't want you to generalize from  
 22 the -- my question to this, the last sentence. So you  
 23 better ask the question separate.  
 24 Q. I don't understand. My question is whether  
 25 this paragraph makes it clearer for you where -- how to

1 A. Okay.  
 2 Q. Does that tell you where to draw the  
 3 distinction between a conserved and a non-conserved  
 4 sequence?  
 5 A. No, again, same answer. This is not my  
 6 territory.  
 7 Q. Let me draw your attention to Column 28,  
 8 Line 64 to Column 29, Line 1.  
 9 MR. GRECO: Column 28? Again, please?  
 10 MR. RABINOWITZ: Line 64 to Column 29,  
 11 Line 1, and we'd better mark the '671 patent as well.  
 12 MR. GRECO: Column 28. Over here.  
 13 MR. RABINOWITZ: Column 29.  
 14 MR. GRECO: 28, right? You started on  
 15 28.  
 16 MR. RABINOWITZ: Sorry, Column 28, Line 64,  
 17 to Column 29, Line 1.  
 18 I'd like to ask the reporter to mark this as  
 19 Exhibit 204, I believe.  
 20 (WHEREUPON, DEPOSITION EXHIBIT 204 WAS  
 21 MARKED FOR IDENTIFICATION.)  
 22 MR. RABINOWITZ: Q. Does that passage from  
 23 the '596 patent tell you anything about where to draw  
 24 the line?  
 25

1 Q. What is your answer to that question?  
 2 A. Well, for a lot of people, I say that is  
 3 tremendous. It's more than million people prevented.  
 4 So what is your question? You want to have  
 5 zero tolerance? Yes, we'd like to have that. But in  
 6 medical practice, there's no such thing as zero.  
 7 Q. In your opinion, are the nucleic acids based  
 8 test for hepatitis C virus infection the best available  
 9 tests for picking up and diagnosing HCV infection?  
 10 A. I don't think the nucleic acid test would  
 11 request an immunoassay. Nobody there can abandon  
 12 immunoassay.  
 13 Q. Are the nucleic acid based tests however  
 14 also an important addition to the public health?  
 15 A. I will say so, yes. But it's the second  
 16 safety net.  
 17 Q. I'm sorry?  
 18 A. Safety net, second. You have to screen  
 19 immunoassay.  
 20 Q. Are the nucleic acid based tests important  
 21 for assuring the safety of the blood supply?  
 22 A. Some way, yes.  
 23 Q. Are the nucleic acid based tests important  
 24 for diagnosing and managing cases of HCV infection?  
 25

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1 Q. What technology does GenProbe's test use?  
 2 A. TMA.  
 3 Q. Apart from TMA, are there other technologies  
 4 that are, in your opinion, as good as PCR?  
 5 A. As I say, I have no experience with the PCR,  
 6 so I don't know. If you are to ask me, say, okay, use  
 7 PCR to abandon immunoassay, I say no.  
 8 Q. I'm restricting my question now to the best  
 9 nucleic acid based tests for hepatitis C virus.  
 10 A. I think the answer is maybe we can find one  
 11 at the Moscone Center, there is an AABB meeting here.  
 12 Because of the deposition, I missed the meeting.  
 13 They will present a lot of nucleic acid  
 14 tests in the meeting, so.  
 15 Q. Based on your knowledge as you sit here  
 16 today, not having attended the meeting, do you consider  
 17 bDNA technology to be as good as PCR technology for  
 18 testing HCV?  
 19 MR. GRECO: Objection. No foundation.  
 20 THE WITNESS: No, I am not here to  
 21 compare the tests. I never run both tests, so it's  
 22 difficult for me to judge.  
 23 MR. RABINOWITZ: Q. You do attend lots of  
 24 meetings.  
 25

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1 A. Could you repeat the question?  
 2 MR. RABINOWITZ: Could you read back the  
 3 question, please.  
 4 (Record read.)  
 5 THE WITNESS: That, you are talking about  
 6 a chronic patient here? You are talking about a  
 7 treatment?  
 8 MR. RABINOWITZ: Q. I'm including  
 9 everything to do with clinical cases of HCV infection.  
 10 A. Some case, yes. Some case, no.  
 11 Q. Wouldn't you agree that PCR-based nucleic  
 12 acid tests are the best available technology for  
 13 nucleic acid based detection of HCV infection?  
 14 MR. GRECO: Objection to the form.  
 15 THE WITNESS: Do you have some other  
 16 tests as good?  
 17 MR. RABINOWITZ: Q. What tests do you  
 18 consider as good --  
 19 A. TMA.  
 20 Q. -- as PCR? Are there any other tests that  
 21 are as good?  
 22 A. The GenProbe test.  
 23 Q. Which test is that?  
 24 A. GenProbe.  
 25

1 hepatitis C, so that is advantage.

2 PCR you have semi-quantitative, but not  
3 necessarily will match to the bDNA. So that is how  
4 much I know.

5 Q. Are you able to say whether or not you agree  
6 that PCR-based tests are the most sensitive for  
7 detecting HCV?

8 MR. GRECO: Same objection.

9 THE WITNESS: That, I don't know. Unless  
10 I just run it, I cannot judge.

11 You have to compare with other, so just only  
12 one say PCR is most sensitive, I have no way to judge.

13 That's why I say, if we go to the meeting  
14 now in Moscone Center, maybe we can find out.

15 MR. RABINOWITZ: Q. Dr. Kuo, does the '596  
16 patent, Exhibit 200, set forth the entire genomic  
17 sequence of HCV-1?

18 A. It just give you the sequence in Figure 1,  
19 so I don't know.

20 Q. Do you know whether or not the sequence in  
21 Figure 1 is the entire, complete sequence of HCV-1?

22 A. I don't think that is important in this  
23 patent discussion here.

24 Q. I'm afraid you will have to answer the

25

1 unimportant questions as well as the important ones.

2 MR. GRECO: He's been doing that all  
3 day, I thought.

4 MR. RABINOWITZ: Q. Do you know whether  
5 Figure 1 sets forth the entire genomic sequence of  
6 HCV-1?

7 A. Figure 1 is --

8 MR. GRECO: Figure 1 of the patent.

9 You're looking at part of Figure 1.

10 THE WITNESS: Right, 1L.

11 MR. GRECO: They have numbers after  
12 them. I don't know what those numbers are.

13 THE WITNESS: That is Figure 1 until  
14 9,000-something.

15 MR. RABINOWITZ: Q. Do you agree that  
16 Figure 1 begins at minus 341?

17 A. Yes.

18 Q. And continues to 9,001, and then continues  
19 for a further line?

20 A. That's correct.

21 Q. Is that the complete genomic sequence of  
22 HCV-1?

23 A. That, I don't know.

24 Q. Does the '596 patent provide the entire

25

1 sequence of any HCV other than HCV-1?

2 A. Well, I didn't read the patent completely,  
3 so I don't know. I think more likely, it's not.

4 Q. So as far as you're aware, it does not?

5 A. Yes.

6 MR. RABINOWITZ: I don't know how long you  
7 want to continue. I've finished at least for the  
8 moment with the '596 patent. I can go on to another  
9 patent, or we can --

10 MR. GRECO: Well, if you're going to  
11 start a whole new area, it's 5:00, maybe it would be a  
12 convenient break time.

13 MR. RABINOWITZ: Okay.

14 THE VIDEOGRAPHER: In the deposition of  
15 Dr. George Kuo, this marks the end of Videotape 4.  
16 Going off record, the time now is 4:59.

17 (Ending Time: 4:59 p.m.)

18

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#### CERTIFICATION

1 I, FRANCES A. WEINROB, duly authorized to  
2 administer oaths pursuant to Section 2093(b) of the  
3 California Code of Civil Procedure, do hereby certify:  
4 That the witness in the foregoing deposition was by me  
5 duly sworn to testify the truth in the within-entitled  
6 cause; that said deposition was taken at the time and  
7 place therein cited; that the testimony of the said  
8 witness was reported by me and was thereafter  
9 transcribed under my direction into typewriting; that  
10 the foregoing is a complete and accurate record of said  
11 testimony; and that the witness was given an  
12 opportunity to read and correct said deposition and to  
13 subscribe the same.

14 Should the signature of the witness not be  
15 affixed to the deposition, the witness shall not have  
16 availed himself/herself of the opportunity to sign or  
17 the signature has been waived.

18 I further certify that I am not of counsel  
19 nor attorney for any of the parties in the foregoing  
20 deposition and caption named nor in any way interested  
21 in the outcome of the cause named in said caption.

22 DATED: NOVEMBER 17, 1999

23

24 FRANCES ANN WEINROB, CSR 4029

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